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The Edward Stirling Lectures.¹

LECTURE I.

WOMEN OVER FIFTY.

By F. A. MAGUIRE,
Sydney.

YEAR by year we shall see in our practices more and more women over the age of fifty years. The advances in public health and hygiene and in the use of antibiotics, the increased knowledge of nutrition and a general advance in knowledge of the problems of health amongst the community are lengthening the allotted life span. One takes the age of fifty as an arbitrary line, as by that time the great majority of women have passed the menopause and are entering into the third stage of their sex life. There are many very real medical and surgical problems to be solved for our patients who are entering this era of life.

MENOPAUSE.

The menopause is due to the cessation of function of the ovaries as glands of internal secretion. The Graafian follicles cease to form, the corpus luteum fails to develop and oestrene and progesterone are withdrawn from the

circulation. Probably in no two women do these phenomena occur in exactly the same way or at the same rate, so that the symptoms of the menopause vary from one patient to another. In sum total, however, the effect is the same.

Alterations in the Anatomy of the Genital Tract.

The vulva and the vagina commence to shrink and lose a certain amount of their elasticity. The mucous membrane becomes dry and there is less secretion from the glands of the vulva and the cervix. The uterus shrinks in size. Gradually the cervix becomes flush with the vaginal vault. The uterus may shrink until it is only two inches by one inch in length and breadth. The ovaries atrophy and may ultimately be less than half an inch in length.

Loss of Oestrogens.

With the loss of the oestrogens there is an alteration in the physiology of the vagina and the vulva. The mucous membrane becomes thin and dry. Very little glycogen is deposited in the cells of the vagina. The acid reaction of the vagina changes to an alkaline one. The pH, which is normally from 5.0 to 6.0, becomes 7.0 or 8.0, and Döderlein's bacilli disappear from the vagina. The elastic tissue in the submucous coats tends to atrophy. All these changes are progressive, so that when the patient reaches the age of sixty or seventy years we may find the parts shrunken and dry. However, these changes are much less pronounced in married women who maintain an active sex life. The normal physiological processes of coitus and orgasm may be retained by many women until at least their seventies.

¹Delivered on June 3 and 5, 1952, at Adelaide.

Nervous Disturbances.

Nervous disturbances consist of (a) flushes, (b) psychiatric problems, and (c) menopausal arthritis.

Flushes.

Most women at and after the menopause complain of what they describe as "flushes". These vary considerably in degree in different women.

The flushes that patients suffer from at this time are probably due to a disturbance of the balance of the endocrine chain, which is seriously disturbed by the cessation of function of the ovary. The pituitary gland, the thyroid gland and the suprarenal gland are also members of this chain. After a few months, in the normal individual, a balance is struck, the flushes disappear and the patient goes on the even tenor of her way.

Severe flushes, however, can be very distressing to a sensitive woman. Such a patient will complain that she is wakened every half-hour or more during the night; she may have to throw off the bedclothes or even jump out of bed. She may be so wet with perspiration that she has to change her nightgown, and every now and again during the day she has a hot flush which causes her to perspire and then she feels hot and cold.

Fortunately the vast majority of Australian women lead healthy open-air lives with plenty of exercise and good food, and it is only in a small proportion that active steps have to be taken to relieve the problems of the menopause.

The degree of reaction of a patient to the menopause is likely to depend on the nervous background with which she is endowed. The quiet, sensible and stable type may go through the menopause without any serious disturbance of any kind; but those women who have a highly sensitive nervous system and are inclined to attacks of migraine or severe nervous headaches may have a very stormy time, with hot flushes for anything up to ten years. If there is an unstable mental background, such as one sometimes sees in women who become mentally upset at their menstrual period or are inclined to go into melancholia, the menopause may be a time of great mental distress and depression. The doctor will always be well rewarded in these cases by a careful study of the personality and mentality of his patient. It pays to talk quietly to these patients for a little while and try to estimate their mental background and stability. It is obvious that the treatment that will suit one will be quite unsuitable for another. The family doctor is very often the best person to make this estimation, as he is familiar with the patient's background and home life. Home worries, domestic upsets, troublesome and inconsiderate husbands and children, business worries, all may play a part in causing excess mental stress and strain in the woman after menopause. The wise and thoughtful family doctor can frequently take steps to help the patient in many ways besides prescribing drugs or hormones.

Psychiatric Problems.

Women who suffer a good deal psychically at the time of the menopause may be seized with suspicions of their husband and accuse him of infidelity or lack of attention or mental cruelty or some such other fault. Such a husband may come to the doctor in a thoroughly puzzled and upset condition. It is our duty then to point out to him quite clearly that his wife is suffering from what is really a mental disease, and that it is not just temper or temperament that is causing the upset. Fortunately in a great majority of cases sympathy and understanding over this time very soon settle the mental difficulty, and the woman comes back to a more normal state of mind.

Menopausal Arthritis.

A condition that is often unrecognized at this time of life is one that has been described as menopausal arthritis. It has to be distinguished from infective arthritis, rheumatoid arthritis and osteoarthritis. There is in these cases no history of infection, and it is definitely associated with the post-menopausal period. The patient complains of

pain in the fingers, in the feet or in the knees. Her knees and the lower part of her back will feel stiff on rising from a sitting position if she has been sitting for some time, and in some patients one will find nodules on the distal joints of the fingers. It is a very real and troublesome condition, but yields easily and quickly to treatment with oestrogens.

Treatment of Menopause.

The first and most important step in treatment is to explain to the patient what is happening and why she is having her symptoms. She should be informed that it is a physiological process through which all women go. So many of these patients have been scared by "old wives' tales" that the change of life is something to be dreaded; they fear that they will put on weight, that they will become obese and unsightly, that they will become hirsute, that they will lose their feelings and desires; and many women feel that they have more or less come to the end of their usefulness when they have arrived at "the change". A brief and clear summing up of the mental and physical changes that are actually taking place in the body, together with an assurance that none of these dreadful things will happen, is frequently sufficient to set a patient in an entirely different frame of mind. Be careful of using oestrogens indiscriminately at this stage. A little oestrogen given with discretion in limited doses over a limited time will give great relief to many of these patients, particularly those with mild arthritis or with severe flushes. Tablets (0.3 milligramme) of dienoestrol should be given three times a day for one month, then twice a day for two months and then daily for three months, with special instructions that the treatment is not to be repeated beyond this time except on the instructions of the doctor. I have encountered many cases in which patients have gone on taking oestrogens for two, three or more years, with the result that they have set up severe post-menopausal bleeding. Be particularly wary of the use of androgens. Some authorities prescribe androgens freely at this time; but an excess of androgens will produce a deepening of the voice and a development of excess hair on the body and face. If for any good reason you wish to prescribe androgens, warn the patient of the possibilities and insist on seeing her yourself at least once a month. I have in the last two years seen three women who continued taking androgens for a considerable period of time, with results that were very distressing to them physically.

For patients who are suffering from nervous disturbances mild sedatives of the type of phenobarbital or bromides or chloral hydrate may be used for limited periods. It is very important to check the diet; see that the patient is getting an adequate amount of necessary vitamins and minerals. A recent survey in America showed that 40% of the population were lacking in adequate supplies of vitamins and minerals in what the patients themselves considered to be a good diet. As some patients gain a little weight after the menopause, it is necessary to check the weight and the blood pressure regularly. I have found that many women about the menopause have a rise in blood pressure up to 170 or 180 millimetres of mercury, systolic. The blood pressure generally settles down quickly on a mixture containing some bromide, phenazone and phenobarbital, particularly if the weight, which may be raised, is brought back to normal by a proper diet.

The most important thing in the treatment of the menopause is to get the patient back to normal as soon as possible. Once she finds that she is normal again she will have no further trouble.

PATHOLOGICAL CHANGES AFTER THE AGE OF FIFTY YEARS.

Hæmorrhage.

A cardinal rule of gynaecology is that "all bleeding at or after the menopause is cancer until it is proved otherwise". This is a good working rule. There are other causes for hæmorrhage after the menopause, but they are so unimportant compared with cancer that the first duty of the doctor is to exclude cancer. Cancer is the killer. If it is diagnosed early it can be cured in a vast majority of cases. If it comes to us too late, there is not very much in our present

state of knowledge that we can do beyond making the patient comfortable and relieving pain. Therefore it is most important that a very early diagnosis of cancer should be made. Bleeding after the menopause is therefore a most important sign.

Cancer may occur in the vulva, the vagina, the uterus or the ovaries. Cancer in the vulva starts as a local ulcer or a sore which bleeds easily on contact. Very frequently it occurs in the cracks of leucoplakia, but it may occur quite apart from this condition. Therefore any bleeding sore on the vulva must be regarded with suspicion.

Cancer of the vagina may be either primary in the vagina or secondary to cancer of the cervix, of the body of the uterus, or even of the ovary; or it may be the result of invasion from cancer of the bladder or rectum. Any bleeding spot in the vagina after the age of fifty years must be examined with great care and investigated at once. The only sure way to make a correct diagnosis is by biopsy with a report by a competent pathologist.

Cancer of the uterus may arise either in the cervix or in the body. Cancer of the cervix is much more common. The first sign usually is contact bleeding. A friable ulcer or a fungating mass may be found on the cervix, or the cervix may be found to be enlarged and infiltrated. From such a growth one frequently finds a discharge which is watery, somewhat dirty in colour and at a later stage foul-smelling. Pain is a late symptom in all cancer, and particularly in cancer of the uterus. By the time a cancer of the uterus has become painful it is usually inoperable.

Cancer of the body of the uterus shows itself first by a discharge which is watery in character. Bleeding may take the form of an occasional "show" at intervals of two or three days or weeks, but later the bleeding becomes continuous. The body of the uterus is larger than it should be for the patient's age. Remember that the uterus shrinks after the menopause. By sixty years it should be only two-thirds of its normal size. A woman of sixty years who is bleeding from the uterus, and who has a uterus which is the size it should be at forty-five years, is very probably suffering from cancer of the body of the uterus.

Remember particularly that cancer can develop in a uterus which contains fibroid tumours, when the bleeding may be attributed to the fibroid tumours rather than to the cancer. It is estimated that 40% of cases of cancer of the body of the uterus are associated with fibroid growths, and a fibroid growth frequently masks the cancer in the mind of the doctor. Cancer can also occur in the cervical stump after a supravaginal hysterectomy. Unfortunately one not infrequently meets with a case in which the patient has been operated on and has had a supravaginal hysterectomy for a bleeding uterus, when the whole trouble was a cancer of the cervix which had been missed at the original operation. No operation for hysterectomy should ever be carried out without preliminary examination *per vaginam* on the operating table and a curettage to exclude the possibility of cancer either of the body of the uterus or of the cervix. The operation is entirely different when cancer is present. The presence of cancer calls for far more radical and thorough extirpation of the uterus, the Fallopian tubes and the ovaries. When the cervix is the site of the cancer, the upper part of the vagina together with the glands draining these areas must be removed as well—that is, Wertheim's pahysterection should be performed. It is always a melancholy thing when a patient comes back within six months of a hysterectomy with a recurrent cancer which was obviously present at the time of the original operation, but which was missed at that time. Therefore, when you have a patient after the menopause who has bleeding *per vaginam*, look and see where the bleeding is coming from and take a biopsy, either directly from the growth or by curettage if the growth is inside the uterus.

Sarcomatous changes are very rare in fibroid tumours. Not more than 1% of fibroid tumours undergo carcinomatous changes.

Carcinoma of the ovary should be suspected in any patient who has bleeding *per vaginam* and has a lump in the pelvis apart from the uterus, particularly if the

bleeding persists after curettage. The cardinal rule here is that all ovarian cysts and tumours should be removed when diagnosed, as 20% of them are malignant, and no one can say by physical examination in the early or operable stage which tumour will become malignant and which will not. Therefore be safe and remove all ovarian tumours when they are diagnosed.

The Use of Endocrines in Treatment.

There are other causes of haemorrhage apart from cancer. Within the last ten years one has seen more and more patients who have been given endocrines more or less indiscriminately or with a limitless dose, who have developed bleeding from the uterus two or three or five or even ten years after the menopause. The bleeding may occur from the administration of excessive amounts of oestrogen; but it is more likely to occur when the doses have been stopped—the so-called "oestrogen withdrawal bleeding". If bleeding is occurring, always ask the patient whether she has been under treatment, and particularly whether she has had endocrines. If you withdraw the endocrine treatment and find that bleeding stops within a week or two and does not recur, you are safe to leave her alone; but if it persists, do not fail to carry out a diagnostic curettage.

Pyometra.

The cervical canal may be sealed up, owing to senile endometritis, to a degenerating fibroid tumour, or to radium treatment which has been applied to the uterus for either a malignant or a non-malignant condition. The uterus is distended with blood and probably pus as well. Occasionally this fluid leaks through a little opening forced down through the cervix by the pressure in the uterus. In these cases the uterus is always enlarged and generally tender. A uterus that is enlarged, tender and bleeding after the menopause should be removed.

Senile Endometritis.

A low-grade infection with staphylococci or even with *Bacillus coli communis* may ascend from the vagina through a gaping os in a patient who has had an old laceration. The endometrium becomes infected and may be shed in patches. The uterine tissue may bleed through the patches laid bare in this way, or the bare patches may adhere to one another and tend to set up pyometra. The diagnosis is made by curettage.

Endometrial Polypi.

Small bleeding endometrial polypi occasionally occur after the menopause. They can be discovered only by curettage.

Foreign Bodies.

Foreign bodies, such as neglected or forgotten pessaries which have stayed in the vagina for two or three or more years, will give rise to foul discharge and bleeding. I have seen a patient in whom the pessary had ulcerated through into the bladder and the rectum, causing fistulae.

One patient, a single woman, aged seventy years, was sent to me with a diagnosis of carcinoma of the cervix. I, too, was sure it was so until I examined her under an anaesthetic and found a ring pessary that had been put in twenty years earlier and forgotten. Fortunately the whole condition cleared up when the pessary was removed; but it was a very difficult task to get it out.

Tumour of the Ovary.

A feminizing tumour of the ovary, such as a granulosa-cell tumour, must always be thought of when the uterus is bleeding and there is another tumour in the pelvis.

Uterine Prolapse and Ulceration of the Cervix.

Uterine prolapse with benign ulceration of the cervix gives rise to contact bleeding. Curiously enough, cancer of the cervix is rare in prolapse; but a prolapsed uterus from friction and pressure may develop a decubitus ulcer which bleeds on friction. If the patient is put to bed for a few days' rest, douching and packing will heal the ulcer; but if there is any doubt a biopsy should be taken.

Vaginal Adhesions.

Senile vaginal adhesions occur in some women from the age of sixty years on. They can be seen and felt. They break down under the finger as fine adhesions and bleed easily. They heal quickly if the vagina is packed with gauze soaked in any mild antiseptic such as acriflavine.

Fibromyomata.

Fibromyomata of the uterus cause women to go on menstruating sometimes to the age of fifty-four or fifty-five years. But remember that 50% of bleeding uterus with fibroids in them also have cancer in them as well, so look with grave suspicion on any uterus with fibroid tumours that is bleeding in a patient aged over fifty years.

Discharge.

Apart from cancer, discharge is uncommon after the menopause. The two common causes of discharge in younger women—gonococci and trichomonas infections—are rare after the menopause; but they should be thought of if the patient has a profuse yellow discharge. The discharge should be examined by a pathologist for signs of either of these organisms and the appropriate treatment applied.

The two other common conditions, apart from cancer, which cause discharge after the menopause are senile vaginitis and foreign bodies. In both these conditions a yellowish, foul-smelling discharge may develop for months before any bleeding occurs. Both these conditions can be diagnosed by examination with the speculum or by digital examination. Remember that any patient who has bleeding or a discharge should be examined with a speculum in a good light.

Prolapsus Uteri.

Prolapsus uteri frequently starts in the first five years after the menopause. It is apparently due to weakening and stretching of the structures of the pelvic floor when the elastic tissue of the broad ligaments and the cervical ligaments tends to shrink and atrophy. Any stress or strain, such as lifting furniture or carrying heavy weights, may bring the prolapse down quite suddenly. The degree of prolapse may vary from a simple urethrocele with a stress incontinence to a cystocele, or a total prolapse of the uterus together with, in advanced cases, rectocele and hernia of the pouch of Douglas. The condition is due originally to stretching and tearing of the cardinal ligaments, of the structures which form the bladder bed, of the *levatores ani* and of the triangular ligaments. The degree of prolapse and the organ affected are dependent on the amount of damage to these four important structures. It is important to remember that one of the most trying symptoms of prolapse is tiredness. Most patients suffering from prolapse complain that they are always tired or that they are exhausted after a little effort. There is no operation in surgery that gives such a satisfied patient as a well-done repair of a prolapse. The patients feel and look at least ten years younger and are very grateful to their surgeon; but prolapse can be cured only by a thorough knowledge of the underlying causes and of the anatomy of the structures of the pelvic floor and the supports of the uterus and bladder. Repair in the vast majority of cases can be effected from below. It is rarely necessary to open the abdomen.

There are, however, certain cases in which a repair operation is contraindicated. Age is not as a rule one of these. A healthy woman in the seventies can stand an operation for repair just as well as a younger woman; but if there are complications in the cardio-vascular system, if there is high blood pressure, if the patient has advanced renal disease, or particularly if she has any pulmonary condition which gives rise to chronic cough, it is better to treat the patient by some mechanical support.

A ring pessary requires *levatores ani* that are in fair condition and not more than two and a half inches apart. In those cases in which the *levatores ani* are wide apart and badly torn, or in which a ring fails to give support, the patient can be given complete relief by the use of a

Napier stem pessary. The patient can be instructed to put the pessary in in the morning and take it out at night. With ordinary care and hygiene she will suffer no discomfort, nor will it give rise to any discharge or pain. I have several elderly and sick patients who are carrying on in great comfort with a Napier stem pessary. If the cervix is badly infected and inflamed, do not perform any repair operation until you have completely healed it by local treatment.

Any patient with a large prolapse should have rest in bed with daily packing and douching for one week before operation. She should have sedatives at night, and be checked for any degree of anaemia and for any rise in the blood pressure. These conditions should be put right before operation. After operation she should be kept in bed for eighteen to twenty-one days, but should be allowed to move freely as far as her legs and body are concerned from the second or third day. "Trisulphal" cream should be inserted into the vagina after the second or third day to prevent local inflammatory reaction. A catheter should be left in for the first four or six days.

Leucoplakia Vulvæ.

Leucoplakia is a condition in which the mucous membrane becomes thickened, sodden and a peculiar bluish grey in colour. It gives rise to intense itching and irritation. We do not know the actual cause of leucoplakia, although many people suspect that it is an endocrine disturbance. Many patients do not respond to oestrogens administered over a period of two or three months. Dienestrol (0.3 milligramme) may be given three times a day for a month. If at the end of that time there is no relief, it is not much use carrying on with it any further. Local applications, ointments and lotions may be tried, but often are not successful. I have had a very considerable amount of success with these cases by local treatment with deep X rays given by a radiotherapist. I am aware that the text-books state that this may give rise to carcinoma. I have never seen any untoward effect arise from this treatment, and I have treated many patients in this way; but if there is ulceration or cracking with bleeding, the safe treatment is to excise the whole area affected. As there is so much loose tissue underneath, this can be done without any great distortion of the parts. The resulting scar is usually soft and supple and gives no trouble. Do not persist too long in palliative treatment of *leucoplakia vulvæ*, as it is a precancerous condition.

Pruritus.

Pruritus vulvæ is a condition which may cause a patient very acute distress and discomfort. The first thing to remember if any patient complains of pruritus is to test the urine for sugar, as diabetes is one of the common causes. If there is sugar in the urine, antidiabetic treatment will rapidly clear up the pruritus. The next common cause is *leucoplakia vulvæ*, which has already been discussed. There is a neurogenic type of pruritus that is rare and occurs practically only in people with a psychopathic tendency. It is best dealt with by a psychiatrist. Pediculi and threadworms may cause pruritus in patients who are afflicted with these conditions. They should be looked for very thoroughly.

Abdominal Tumours.

Fibromyomata uteri never commence growing after the menopause, but fibroid tumours which are present before the menopause may enlarge after the menopause, owing to degeneration in the tumours or to torsion of a pedicle which causes acute symptoms of abdominal pain and distress. Sarcoma occurs in less than 1%, but always remember that if a uterus with old fibroid tumours starts to bleed after the menopause, carcinoma of the body of the cervix or of the ovary must be suspected. Do not be lulled into a false sense of security by blaming the bleeding onto the fibroid tumours. It is your duty to investigate thoroughly and exclude particularly any malignant condition or any degenerative changes in the tumours. As a general rule, bleeding fibroid tumours call for hysterectomy.

Ovarian Cysts.

Ovarian cysts are not uncommonly found after the menopause. If they are enlarging they should be removed at once and without being ruptured. It is much better to make a large incision and to take great care to remove an ovarian cyst without rupturing it than to tap it, no matter how large the cyst is, as it is almost impossible to say whether or not there are malignant changes in the tumour. The signs of malignant changes in an ovarian cyst after the menopause are rapid enlargement, irregular and nodular outline, and fixation. The presence of free fluid in the abdomen and wasting both indicate that the cyst has ruptured. A ruptured ovarian cyst which is malignant causes rapid deterioration in the patient's condition; but even a ruptured ovarian cyst should cause an exploratory laparotomy to be performed, because occasionally, even though the case looks hopeless, if enough of the tumour is removed the patient may recover for a while at all events.

Bowel Disturbances.

It is very important to remember that any pronounced change in the bowel habits after the menopause in the direction of constipation, diarrhoea or pain should make one think of cancer of the bowel. Cancer of the large bowel is a very quiet, slowly growing condition and sometimes lies quietly in the abdomen for months. In any condition of disturbance of the bowel habits which is causing the patient anxiety or worry or discomfort, examine the patient by X rays, both with an opaque meal and with an opaque enema, to exclude carcinoma of the bowel. Remember particularly that haemorrhoids are often associated with rectal carcinoma. Always satisfy yourself when a patient with haemorrhoids complains of bleeding or enlargement of the haemorrhoids that no carcinoma is present in the rectum. A digital examination should be made in every case; if there is any doubt, the rectum should be examined through a sigmoidoscope.

An anal fissure causes more pain and trouble than haemorrhoids, but it is usually easily cured. Painful bleeding haemorrhoids should be removed. Anal fissures usually yield to treatment with those aperients which give soft motions, together with sedative suppositories and ointments. A starch and opium enema will give these patients great relief. Surgical interference may be necessary.

Urinary Disturbances.

Incontinence of urine in a patient after the menopause varies in degree.

Stress Incontinence.

Stress incontinence is a condition in which the patient passes urine on coughing or straining, on stepping off a pavement, on making a stroke at golf, or in any similar sudden jerky exertion. It is associated with a urethrocele. It is usually relieved by a plastic operation on the urethral supports. It calls for a thorough repair of the triangular ligament or uro-genital diaphragm. Of patients with stress incontinence, 90% can be cured by a properly designed operation performed from below. The sling operation has become fashionable in recent years, but it is very rarely called for and should be performed only by one who is very expert in pelvic surgery. There have been a number of cases of total incontinence and very distressing symptoms as a result of improper performance of this operation.

Total Incontinence.

Total incontinence may be due to a vesico-vaginal fistula. Examine the vagina thoroughly with a good light. Dyes such as methylene blue may be given by mouth, or they may be passed into the bladder through a catheter. The dye may be seen escaping into the vagina. Sterilized milk may be used in the same way. Thorough exposure and a good light will generally find a fistula if it is present. It may be due to malignant disease or a foreign body; it may follow the use of radium; it may follow a hysterectomy or

a plastic operation on the vault of the vagina or for prolapse. The condition can usually be cured by operation.

Remember, however, to examine the nervous system thoroughly, as occasionally total incontinence is due to a disease of the nervous system, when operation, of course, will be worse than useless.

Prolapse of the Urethra.

Prolapse of the urethra may be painful and distressing. A dark red bulging mass is seen in the position of the urethra. The urethral canal will always be found in the centre of the mass, which is dull red and not tender. Very rarely the prolapsed mass becomes gangrenous. It may then be mistaken for a melanotic sarcoma. I have encountered two such cases.

Urethral Caruncle.

Urethral caruncle is comparatively rare. It is a small growth which is brilliant scarlet red in colour with a shiny surface, and is acutely sensitive to touch. It bleeds easily from pressure. The patient complains that she is tender in the parts and that she sees blood on the towel. The diagnosis is made by seeing the tumour. The lesion is very likely to recur unless it is removed widely. Fortunately it is rarely malignant.

CONCLUSION.

In dealing with aged women, be very patient with them; take time to find out what their real trouble is. Some of them are slow in their mental processes and vague in their answers; but patience, perseverance and kindness will generally enable you to get to the root of their complaints. Give them relief and comfort; relieve pain; do not withhold sedatives; ensure sleep. See that their diet is adequate and suitable for their age. Remember always that their pelvic condition may be secondary to some other general medical and surgical condition; pruritus may be secondary to diabetes; prolapse may be secondary to an abdominal tumour; bleeding may be secondary to a blood dyscrasia. Finally, as an eminent gynaecologist once said: "Always be kind to women, they have a lot to put up with."

MURRAY VALLEY ENCEPHALITIS: COMPLEMENT-FIXATION TECHNIQUES.

By MARGARET DONNELLEY AND E. L. FRENCH.

From the Department of Experimental Medicine,
University of Melbourne, and the Walter and
Eliza Hall Institute of Medical Research,
Melbourne.

A DESCRIPTION of the 1951 epidemic of Murray Valley encephalitis (MVE) has been published recently (Anderson, 1952; French, 1952; Robertson, 1952; Robertson and McLorinan, 1952; Anderson, Donnelley, Stevenson, Caldwell and Eagle, 1952). The present paper gives details of the ice-box technique of complement fixation adopted for the titration of large numbers of human and animal sera. All the complement-fixation titres reported in the above series of papers were determined by the method described below.

Preparation of the Complement-Fixing Antigen.

The virus of Murray Valley encephalitis was originally isolated from a human brain by inoculation on the chorio-allantois of eleven-day chick embryos (French, 1952). In this situation growth of MVE virus produces large amounts of complement-fixing antigen.

Throughout the investigation uniform preparations of antigen were obtained by always using the same stock virus to prepare the inoculum for the eggs. The stock was derived in this way. Infected membranes from the primary isolation were passed to further eggs of the same age; the

second egg passage material was inoculated into three weeks old mice by the intracerebral route. An emulsion of mouse brains from the fourth intracerebral mouse passage was stored in capillaries in 0.05 millilitre amounts at -70° C. and comprised the stock virus material. Each week one capillary was taken, diluted one in 10 in broth containing penicillin and streptomycin, and inoculated intracerebrally into three-weeks-old mice. After four days at least two of the mice were killed; their brains were ground with alumum and then suspended in five millilitres of beef heart infusion broth. The emulsion was centrifuged for ten minutes at 2500 revolutions per minute and a one in 30 dilution of the supernatant was made in broth containing penicillin and streptomycin. This fresh mouse brain suspension was inoculated onto the chorio-allantois of ten-day-old chick embryos, which were then incubated for forty to forty-two hours at 35° C. The membranes were harvested and ground together with the drainings, and the suspension was extracted with calcium magnesium saline¹ in a volume of one millilitre for every ten membranes. The suspension was centrifuged at 3000 revolutions per minute for thirty minutes at bench temperature. The resulting supernatant served as the virus antigen.

A chorio-allantoic membrane suspension from uninoculated eggs of the same age served as control antigen.

The Test Proper.

The micro technique of Donnelley (1951) for influenza was followed closely, except that it was found necessary to allow the complement fixation to go on overnight at 4° C. rather than for one hour at 37° C. Calcium magnesium saline was the diluent, and fresh guinea-pig complement diluted to contain three 50% haemolytic doses (3HD₅₀) and 3% sheep cells sensitized with 8HD₅₀ of haemolysin were used. All sera were heated in their initial dilution at 62° C. for fifteen minutes before use.

With a Pasteur pipette delivering 25 drops per millilitre of saline, single drops of antigen, serum and complement were mixed in tubes of the Wassermann type (7.5 centimetres long and of 0.8 centimetre internal diameter). The racks were placed in the refrigerator overnight and the next morning were warmed for five minutes in a water-bath at 37° C. before the addition of one drop of sensitized cells to each of the tubes. The racks were then incubated in the waterbath at 37° C. for thirty minutes, and the result was read; 50% haemolysis was taken as the end-point.

The complete test consisting of titration of complement, standardization of antigen and titration of sera took two and a half days. On the first day freshly washed sheep cells were sensitized with haemolysin and complement was titrated, the short incubation period (that is, 37° C.

¹ Calcium magnesium saline was prepared as follows: sodium chloride 8.50 grammes, magnesium chloride 0.192 gramme, calcium chloride 0.0275 gramme, boric acid 1.203 grammes, sodium borate 0.052 gramme, distilled water to one litre.

for one hour instead of 4° C. for eighteen hours) being used. These reagents were then used over the complete course of the test, the complement titre being checked daily.

On the first afternoon freshly prepared MVE antigen was standardized as described below and the result was read the following morning. On the second afternoon test sera were titrated (see below) and the results of these titrations were read on the third morning.

Standardization of Antigen.

Chess-board titrations of standard "positive" and "negative" human sera were made with fresh preparations of the MVE and control antigens, the dilutions shown in Figure I being used. Complement was added and after overnight fixation at 4° C. and thirty minutes' haemolysis at 37° C. the result was read.

As is shown in Table I, no reaction occurred when the "positive" and "negative" sera were titrated in the presence of the control antigen, nor when the MVE and control antigens were titrated in the presence of the "negative" serum. On the other hand, a good reaction was shown when the MVE antigen was titrated against the "positive" serum.

From such a test the optimal dilution of antigen for use in the titration of sera was selected. In Figure I the highest dilution of MVE antigen giving a maximal antibody titre for the "positive" serum is 1:8. Accordingly a 1:8 dilution of MVE antigen would have been made up in this case and the control antigen diluted similarly.

Although successive batches of MVE antigen gave this result consistently, the standardization procedure was always carried out. For this purpose small volumes of a serum with a high antibody titre and of a "negative" serum were frozen and dried *in vacuo*, and as required were reconstituted and used as standard sera.

Titration of Sera.

All sera to be tested were diluted 1:5 in calcium magnesium saline and heated at 62° C. for fifteen minutes. Doubling dilutions of these were made in duplicate, by the use of the dropping technique described previously (Donnelley, 1951). To one set the optimal dilution of the MVE antigen was added, and to the other the similarly diluted control antigen. The standard "positive" and "negative" sera were included as controls of the sensitivity as well as of the specificity of the test.

Again, after overnight fixation at 4° C., warming of the racks and addition of sensitized cells, the results were read after thirty minutes of haemolysis. The reciprocal of the dilution showing 50% haemolysis was recorded as the antibody titre of a serum. Occasionally, however, a serum showed a reaction with both the MVE and the control antigen, and in such instances the result was recorded as non-specific.

TABLE I.
"Chess-board" Titrations of an Acute and Convalescent MVE Serum with an MVE and a Control Antigen.

MVE Antigen Dilutions.	Serum Dilutions. ¹								Control Antigen Dilutions.	Serum Dilutions. ¹							
	1/5	1/10	1/20	1/40	1/80	1/160	1/320	1/640		1/5	1/10	1/20	1/40	1/80	1/160	1/320	1/640
Acute MVE Serum.																	
1/2	0	0	0	0	0	0	0	0	1/2	0	0	0	0	0	0	0	0
1/4	0	0	0	0	0	0	0	0	1/4	0	0	0	0	0	0	0	0
1/8	0	0	0	0	0	0	0	0	1/8	0	0	0	0	0	0	0	0
1/16	0	0	0	0	0	0	0	0	1/16	0	0	0	0	0	0	0	0
Convalescent MVE Serum.																	
1/2	4	4	4	4	4	4	4	0	1/2	0	0	0	0	0	0	0	0
1/4	4	4	4	4	4	4	4	1	1/4	0	0	0	0	0	0	0	0
1/8	4	4	4	4	4	4	4	1	1/8	0	0	0	0	0	0	0	0
1/16	4	2	0	0	0	0	0	0	1/16	0	0	0	0	0	0	0	0

¹"4" = 0% haemolysis; "2" = 50% haemolysis; "1" = 75% haemolysis; "0" = 100% haemolysis.

being complete checked antigen was test these nega- in after sys- the ence control "live" own "live" for the anti- tingly this was f a "ve" red ag- es. by sly he nd ity of real as a he as

Titration of Animal Sera.—The test so far described applies to human sera. As the need arose it was extended to horse, dog, cattle, sheep and pig sera, and later to fox and opossum sera by Miss M. Eagle of this institute. Of these species, horse, dog, fox and opossum sera yielded positive titres with some non-specific reactions, particularly pronounced in dogs. The remaining species gave negative or slightly non-specific results. As with human sera, small volumes of "positive" and "negative" serum from each species showing positive reactions were stored for use as standards, and before sera from any one species were titrated, the MVE antigen was standardized against the standard "positive" and "negative" serum of that species.

Limits of Variation of Factors.

Antigen.—It has already been mentioned that uniform batches of antigen could be produced only if the same stock virus was used to prepare the inoculum for the eggs. Other variables were the age of the eggs inoculated with the virus and the time of incubation of these eggs. Eggs incubated at 39° C. for nine to seventeen days before inoculation with MVE virus were harvested after forty-two hours' incubation at 35° C. and the chorio-allantoic membranes were tested for complement-fixing antigen. It was found that the titre of the complement-fixing antigen fell off sharply in eggs older than twelve days before inoculation. Eggs that had been initially incubated for ten days at 39° C. before inoculation were found to yield antigen in optimal amounts. In addition, chorio-allantoic membranes harvested eighteen, twenty-four, forty-two and sixty-six hours after inoculation were examined for antigen. No complement-fixing antigen was detected at eighteen or twenty-four hours, but a maximal titre was found at forty-two hours with a decline at sixty-six hours. From these data the conditions for the routine preparation of the MVE and control antigen were selected.

Time of Fixation.—The greater sensitivity of overnight fixation at 2° to 4° C. in certain virus systems was originally described by Bedson and Bland (1929), and confirmed by Casals and Palacios (1941). The latter workers were specifically concerned with the diagnosis of virus infection of the central nervous system by the complement-fixation test. In the present investigation, the complement-fixation phase of the test was initially carried out at 37° C. for one hour with an almost negative result. By employing a period of about eighteen hours at 2° to 4° C. in a refrigerator for complement fixation, the reaction was enhanced approximately eight times without the introduction of non-specific effects. This technique was obviously preferable, even though it meant increasing the over-all time of the test from one to two and a half days.

Assessment of Test.

In order to determine the specificity and sensitivity of the test, the serological results were viewed in terms of clinical findings, and in addition large numbers of presumed normal sera (for example, from members of the staff of this institute) and of sera from patients in Melbourne hospitals convalescing from various illnesses were included in the titrations.

The results have been discussed in the above series of papers; but in summary it may be said that of the 40 clinically diagnosed cases of Murray Valley encephalitis 33 were examined serologically. In 30 complement-fixing antibody developed, and in three the results were negative. Two of the three patients designated as "negative" died, possibly before antibody appeared in the circulation, whereas the remaining patient (Case XVII¹) had not developed antibody as late as the sixty-first day after the onset of illness. In marked contrast, there were no "positive" sera among 27 patients clinically diagnosed as suffering from "other central nervous system infections" who had not been in the MVE epidemic area, nor among 44 healthy residents of Melbourne. Sera examined from a number of patients in Melbourne convalescing from influenza and mumps were uniformly "negative".

¹ Case XVII corresponds with that quoted in the previous paper of Anderson (1952).

In those species of animals exhibiting "positive" sera, the great majority of "positive" sera came from animals in northern Victoria—a known epidemic area. Only an occasional "positive" specimen of serum was received from southern Victoria, where there was no other evidence of the presence of MVE virus.

Discussion.

For the epidemiological study of MVE it was essential at the outset to develop a laboratory test for the detection of serum antibody. A requisite of such a technique was that it should be sensitive and specific. Further, it was desirable for it to be economical in time and materials so that large numbers of titrations could be carried out rapidly. For this reason an in-vitro test was preferable to an in-vivo test.

The egg membrane complement-fixing antigen originally produced by French (1952) was very satisfactory. Standardization of this antigen with human and animal sera consistently gave the optimal dilution of antigen as one in eight. The technique adopted for the titration of sera was a slight modification of the micro technique of Donnelley (1951) for influenza. As in the original technique, a minimal excess of complement (3HD_{50}) was sufficient to eliminate non-specific effects under the conditions of the test, so that high sensitivity was maintained.

An assessment of the test in the early stages of the investigation indicated a satisfactory degree of sensitivity and of specificity, while the survey of the figures for the complete investigation (Anderson *et alii*, 1952) gave full support to this finding.

Summary.

A technique is described for the estimation of complement-fixing antibody to Murray Valley encephalitis virus.

The antigen is a simple saline extract of infected chorio-allantoic membranes, and is satisfactory for human and mammalian serum titrations.

The ice-box modification of a previously described volume-dropping technique provided a simple complement-fixation test giving highly sensitive and specific results.

The test detected complement-fixing antibody in human, horse, dog, fox and opossum sera. Sheep and cattle sera tested gave negative results.

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THE AETIOLOGY AND TREATMENT OF
HYPERTENSION.¹

By IAN SIMPSON,
Sydney.

THE great variety in the theories on the aetiology of hypertension is apparent even on brief acquaintance with some of the voluminous literature on the subject. There seems to be a tendency to exclude this or that factor because it fails to provide the complete explanation. This is probably the result of attempts to over-simplify what is, in fact, a highly subtle and complex regulatory mechanism. Rather than attempt to cover the whole field, I have restricted my remarks to certain aspects of the essential type of hypertension.

Hypertension has been usually regarded as a disorder largely confined to occidental civilization. Smirk (1949) has perhaps helped to confirm this impression by his experiments, in which he claims to have produced hypertension in rats following exposure to the continually recurring blast of a "Kluxon" horn. Particular significance has been placed on the studies of the American southern Negro, who, after 200 years' contact with our culture, is said to have acquired an incidence of the disease about three times that of his neighbouring white American. Yet Dubois (1932), in a study of Congo natives, reported an incidence of 35%, and Sanders (quoted by Goldblatt) found a very high incidence in the Negro population of the Virgin Islands. These islands have a 95% black population who do not live in competition with the white man. However, in spite of these views, it is obvious that in our civilization the maturing individual gradually becomes more and more confronted with the complex problem of maintaining his and his family's existence, prestige and position—tasks that unavoidably invoke hostile competitive feelings and fears, at the same time requiring an extreme control.

I, for one, have yet to be convinced that a particular personality has any specific aetiological significance. Well-controlled investigations (Gressel *et alii*, 1949) invariably show that the so-called characteristic personality is not exclusive to the disease. Saul (1939) found patients without hypertension who had the same conflicts as hypertensive patients, but who had nevertheless found workable solutions for their difficulties. He suggests that it is not the conflict itself but the individual's specific reaction to the conflict that may be peculiar to hypertensive patients. The conflict commonly found is that between hostility, aggression and rebellion on the one hand and submissiveness, desire to conform and dependence on the other. Saul holds that in hypertensive patients the hostility is intense, chronic, close to consciousness, not adequately repressed, but at the same time inhibited. It finds no outlet in behaviour, in sexual activity or in an organized neurosis.

This conflict is seen in patients whose history often reveals that from an early age they have lacked the ability to confide and have had an ambivalent attitude towards their parents and a conflictual attitude towards siblings. As children they were shy, and had stiff, domineering mothers who demanded compliance and who refused to tolerate outbursts of anger. In the home they have been forced to compete for affection and approval by being good and by conforming. Frequently they have been thrust prematurely into situations of self-reliance. As adults, they present a gentle, easy-going and amiable facade, but underneath they are tense, suspicious, defensive and ready to fight, but afraid to do so. Their attitudes and their circulatory physiology are mobilized for combat, but they do not engage in it against the pertinent adversary because of a guilty fear of consequences. They show a need to conform and keep the peace and are continually afraid they will not succeed. As a result they are preoccupied

with a need to save face. Dunbar considers that a common reaction to their discovery of their hypertension is an attitude of exaggerated fear combined with a relief in having an alibi for failure. This "alibiology", as she calls it, is not limited to cases of hypertension. Unfortunately it is fairly common in most chronic illnesses, and can usually be assessed if we ask ourselves the question, "what meaning has the illness for this particular individual?" I have known the reaction for some years as the "if only" syndrome". Dunbar regards hypertensive patients as perfectionistic, highly ambitious, but over-cautious and fearful of not making the grade. Consequently they have difficulty in making decisions and tend to court more responsibility than they are capable of handling. Alexander (1939) points out that the prominent personality traits are those with survival value in our competitive cash culture. The patients' difficulty appears to consist in reserving the biological mobilization for short-term emergencies in which it is appropriate, instead of adopting it as a way of life. A common impression is their readiness to develop a sense of injustice resulting in many difficulties with authority. They leave their jobs because they cannot tolerate what they consider to be "stand-over" tactics by the foreman or because they are overlooked for promotion. However, in spite of the many personality studies, as yet we have no evidence which helps us to anticipate which individual in a given situation will develop hypertension, which will develop peptic ulcers or colitis, which will become an alcoholic or which will join the church.

In all probability the role played by emotional and mental stress in the genesis of hypertension is purely an accessory one, though a more fundamental role has been suggested by some authors. The fact that acute emotional excitement may result in transitory and emergency-like elevations of blood pressure is in itself no proof that long-standing emotional states can precipitate chronic vasoconstrictions.

In laboratory animals Selye (1950) has produced evidence which indicates that hypertension may be one of the diseases of adaptation. His broad approach affords much food for thought, but it offers no explanation of the initial pathway through which stress-producing agents act on the hypothalamic vegetative centres and the pituitary, where he holds that the systemic defence measures are coordinated.

Reiser and his associates (1951) consider that the more intensive the study, the higher the frequency of correlation between emotionally stressful life situations and the onset, the symptoms and the complications of hypertension. In a close study of 12 cases they conclude that even the precipitation of the malignant phase could be chronologically correlated with such situations or events. They point out that the blood pressure in hypertensive patients does not necessarily rise in response to stress. It may even fall, for when a reaction of mobilization was not evoked and the subject, on the other hand, felt defeated and overwhelmed, a depressor reaction occurred. These authors also noted a difference in responses to the cold pressor test in the same subject when the patient knew that the outcome would determine whether or not he was to be submitted to sympathectomy.

In an interesting study of the relationship of emotional tension, blood pressure and renal blood flow, Wolf and his associates (1948) found that it was invariably possible, by introducing topics which aroused serious conflict, to bring about a sharp rise in systolic and diastolic pressures and a limitation of renal blood flow which usually outlasted the blood pressure rise. Over all, the hypothesis that seems most attractive is that these patients are hypersensitive to threats of danger and insecurity because the defences and compensations they erect as counter to anxiety are consistently inadequate. It is not so much the catastrophic events that are important as the sustained over-reactions to the minor stresses of daily life.

The relationship between a susceptibility to transient hypertensive episodes during stress and the pathogenesis of sustained essential hypertension is still not clear. In a statistical analysis of medical records of 22,741 army officers

¹ Read at a meeting of the New South Wales Branch of the British Medical Association on September 25, 1952.

Levy and co-workers (1945) conclude that such transient hypertension is often a precursor of hypertensive vascular disease. Many authors have pointed out the differences between the so-called neurogenic hypertension and essential hypertension (see Table I).

It is possible that emotionally initiated sympathetic adrenal activity may cause repeated episodes of renal vasoconstriction and ischaemia and hypertension which finally lead to the development of local changes capable of permanently altering the renal haemodynamics or renal metabolic activity. Evidence is accumulating that indicates that the kidney may be first the victim and later the culprit in the same case. Volhard (1948) suggested that the link between neurogenic and essential hypertension was the gradual exhaustion of the reflex vasodilator mechanism in response to recurrent stresses which raise the cardiac output. Unfortunately there is no reliable test which will measure vascular reactivity accurately or consistently enough for it to be used as a means of determining the probability of future hypertension in an individual case.

TABLE I.

Observation.	Essential Hypertension.	Neurogenic Hypertension.
Pulse rate	Normal.	Increased.
Cardiac output	Normal.	Increased.
Total peripheral resistance . . .	Increased.	Normal.
Blood pressure fluctuations . . .	Marked early, limited late.	Marked.
Blood flow in extremities . . .	Normal.	Increased.

Platt (1948) considers that his evidence is compatible with the hypothesis that essential hypertension is an hereditary disease conveyed by a Mendelian dominant with a rate of expression of more than 90%. He has little time for loose statements on the importance of environmental factors, especially psychological trauma, on the development of the disease. With this I agree; but perhaps Platt, in considering psychological trauma *per se*, has overlooked the more subtle influences of the minor stresses in day-to-day living and the manner in which certain individuals deal with them. The implication is that the hypertensive individual and his clan may meet life's stresses in a particular way and in a different way from members of other stocks. Platt has also emphasized the fact that hypertension, and in particular malignant hypertension, in young people was rarely essential, but nearly always secondary to causes elsewhere, especially in the kidney.

Treatment of the hypertensive patient should be aimed at an improvement of functional capacity, symptomatology and general well-being, as well as lowering the blood pressure and extending the duration of life. There is sufficient evidence that hypertension itself is harmful to make a reduction of pressure desirable; but this alone does not constitute an adequate or satisfactory treatment for the disorder. A brief review of the efforts made to bring the blood pressure down is given by Weiss, whom I quote:

Because of an ill founded idea that protein is responsible for hypertension and kidney disease, he (the patient) is denied meat, especially red meat, which for some reason is looked upon with particular dread. Then his diet is rendered even more unpalatable by the withdrawal of salt. One would sympathise with this half-starved victim of good intentions except that he probably would not be able to eat anyway, his teeth having been removed on the theory that focal infection has something to do with hypertension. Even before this period he has sacrificed his tonsils and has had his sinuses punctured because of the same theory. In case he actually had been able to eat some solid food in spite of these therapeutic measures, the slight colonic residue was promptly washed out by numerous

colonic irrigations, especially during the period when the theory of auto-intoxication was enjoying a wave of popularity. To add to his unhappiness, he may be told to stop work and exercise and, of course, is denied alcohol and tobacco as well as coffee and tea. And now, to cap the climax of his difficulties, the unfortunate person with hypertension has been referred to the neurosurgeon who is prepared to separate him from his sympathetic nervous system.

To these measures may be added the administration of thiocyanates, pyrogens and veratrum alkaloids, the use of which seems to encroach upon the sphere of the toxicologist.

Most authorities now agree that an attempt to lower the blood pressure by the present means available is indicated only in the premalignant and malignant varieties. Although the height of the blood pressure is not necessarily an accurate index of the severity of the basic disease process or of the prognosis, there does not appear to be any evidence that a symptom-free patient who has essential hypertension and a diastolic pressure of, say, 115 millimetres of mercury or less would be better off prognostically if the pressure was reduced to 80 or 90 millimetres. The therapeutic hazard in a disease should not exceed the disease hazard. This maxim should be remembered when the use of some of the more modern drugs is being considered, for these drugs, when used in doses sufficiently large to lower blood pressure appreciably, frequently worsen the condition of the patient and may even induce the alarming manifestations of local thromboses.

If symptomatic improvement is desired, then any form of treatment which is prescribed with enthusiasm and conviction will achieve success in a large percentage of cases. Ayman (1931) proved this to be so in 82% of his cases by using dilute hydrochloric acid. He also showed that most of the early symptoms of hypertension are quite unrelated to the level of blood pressure. Incidentally, he was unable to find amongst his patients a headache that might be termed characteristic. His studies indicate the fallacy of using the disappearance of headache and other subjective symptoms in the evaluation of the treatment for the disease. These symptoms are frequently the main cause of the disability—a disability that is often out of all proportion to the disease. It is dangerous to give a label to a set of symptoms until you are convinced that it is the right one. If we meet with the syndrome of headache, palpitation, giddiness, fainting, fatigue, constriction in the chest and hyperventilation (often called breathlessness by the patient) and call it "hypertension" because the blood pressure is found to be raised, then a suggestion is implanted in the patient's mind which fixes his worries and anxieties in an almost indelible fashion. If the blood pressure, on the other hand, happens to be normal, we call this syndrome "a neurosis". It is so easy to strap on a blood pressure cuff and say "it's your blood pressure", and more difficult to spend time and find out the emotionally disturbing factors that so often act as precipitants of such symptoms.

Wolf and Wolff (1946) have demonstrated the failure of exercise to elevate blood pressure more in hypertensive than in non-hypertensive subjects, and they criticize the restrictions frequently prescribed. The phrases "take it easy" and "go home and rest" are often interpreted by the patients as meaning that they are on their last legs. Many of them are very unhappy in hospital. If their admission is required for investigation, the tests to which they are submitted should be explained to them and carried out promptly. It is never wise to tell them too far ahead of any particular test, and above all their cases should not be discussed at their bedside.

A psychological approach does not apply to all hypertensive patients, and no study that I know suggests that psychotherapy can alter the eventual course of the disease or lower the mortality. But disability as well as blood pressure can be reduced by such means. Psychotherapy implies a more adequate approach to the problem than the almost universal three half-grain doses of phenobarbital, the drug which has become the national food of civilization. One of the chief effects of this is to remind the patient three times a day that he has the disease which

causes cerebral accidents, paralysis and death. Similar remarks could apply to diets prescribed and motivated by fear. The more enthusiastic will supplement this treatment with the advice "not to worry", which is of little value when no concerted effort is made to find out the chief sources of such worry. How can a patient refrain from worry if his attention is constantly focused on his blood pressure by the over-zealous use of the sphygmomanometer and he is preoccupied with the ideas of a stroke, heart failure and kidney disease? The dismissal of the patient with the profound statement that his symptoms are all due to his nerves is to leave him prey to many unwholesome thoughts. These are chiefly directed towards the doctor, for the patient gains the idea that the doctor believes his complaints are imaginary.

Psychotherapy is primarily directed towards the improved functioning of the individual in his environment rather than towards the unachievable goal of a cure for a disease for which there is no cure. Its object is to understand the motivations and mechanisms of disturbance of function and to assist the patient to handle his personal and environmental problems in a more satisfactory way. Although we are dealing with "tender vessels" who need protection from strain, especially from demands upon a self-reliance they do not possess, it is important to encourage a reasonable programme of work in keeping with the disability and to reeducate them along the lines of "carrying on". If the patient is encouraged to talk about himself as a person rather than as a medical "case", and if he is allowed to air his emotional problems, he is often able to get a better perspective of them.

Reiser and his associates (1951) consider that the most important aspect of the treatment situation is the doctor-patient relationship. Patients certainly respond to the inner attitudes and feelings of the physician, who should attempt to play the role of a strong, thoroughly dependable, authoritative fellow man—one who is capable of disinterested affection and able to share the patients' anxieties without adding to them. The first step is to discover and correct the patients' misconceptions and treat their secondary anxieties. They often do not really know how much they are disturbed, but are apt to project their worries into questions about their blood pressure, heart and brain. They need to be weaned away from an over-concern with the level of their blood pressure and taught the truth about their condition in small, easily assimilated doses. Encourage them to release their tension and express their aggression along the socially acceptable lines of directed work, play and physical exercise compatible with their local culture, physical state and age. Help them to recognize that they feel threatened, angry and anxious, and indicate how they may abandon their costly inappropriate emergency patterns of reaction and deal with threats and challenges in a more direct and constructive fashion. One phase of their emotional disturbance which frequently requires attention is the inhibited sexual development with actual or relative impotence and a tendency to failure in heterosexual adjustment. Although this may be stressed after sympathectomy, it can often be found to exist in some degree before this event if the case is fully investigated.

The methods of psychotherapy will naturally vary according to the individual, but apparent lack of insight by the patient is not of much significance because the ability to formulate frequently lags behind a changed behaviour.

The criteria by which some therapeutic results have been evaluated have often been extremely questionable. The fallacy of using relief of subjective symptoms in this evaluation has already been indicated. If the level of blood pressure is the chosen criterion, then its level needs to be assessed repeatedly over a long period before and after treatment before any conclusion should be reached. There is also some conflict as to the minimum drop of pressure that can be regarded as significant. Statistical analysis of life expectation gives little indication of the outcome in an individual case. This criterion is offered by

Smithwick in support of sympathectomy, but all tests to improve selection in individual cases have failed.

In conclusion, let us keep in mind the possibility that the fears we invoke and the cures we prescribe may be worse than at least some forms of the disease.

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THE AETIOLOGY AND TREATMENT OF HYPERTENSION.¹

By JAMES ISBISTER, M.R.C.P., M.R.A.C.P.,
Sydney.

In this paper I propose to say little about the causes of essential hypertension, but to stress more the causes of secondary hypertension, which is so often confused with the essential or primary form. I then wish to consider the various methods of treatment which are advocated, unsatisfactory though they are.

The first essential in the consideration of this subject is to define hypertension. There is great difference of opinion in regard to this. Obstetricians would have us call any person whose blood pressure is above 120 millimetres of mercury (systolic) or 80 millimetres of mercury (diastolic) hypertensive. Life assurance companies usually accept 140 millimetres of mercury (systolic) and 90 millimetres of mercury (diastolic) as the upper limit of the normal range. Others again allow 160 millimetres of mercury (systolic) and 100 millimetres of mercury (diastolic) as the limit of normal, some variation being made for age. I place myself in this group. The extremely liberal view is to insist as well on some evidence of hypertensive vascular disease affecting the heart, the kidneys or the retina. This great variation in the definition of hypertension accounts for the differences of opinion one meets regarding aetiological factors and management. Personally I feel that far too many patients with 170 millimetres of mercury, systolic pressure, and 110 millimetres of mercury, diastolic pressure, at a single reading have been treated for hypertension, with resultant great harm.

Aetiology.

Essential Hypertension.

The exciting cause of essential hypertension is unknown, but certain predisposing factors are important. These have been studied in Australia by Hetzel (1951), who found that this group comprised 89% of a series of 203 patients. Hetzel found that obsessional compulsive personality traits were present in 50% of both the male and female patients, and appeared to be a major factor. He found that toxæmia of pregnancy had previously occurred in 53% of the parous women, though these women may have developed hypertension in any case at a slightly later age. Hetzel further found hereditary influence present in 43% of the women, but in only 19% of the men. In contradistinction to these figures, Platt (1947) found that about 80% of patients with essential hypertension had a "positive" family history. About 30% of his patients had secondary hypertension, and of these only about 40% had a "positive" family history.

Secondary Hypertension.

I should like to stress the importance of the diagnosis of secondary hypertension in an individual case, as the course and management may be so different. On the whole this type appears clinically in the younger age group, under forty years, and there is a much higher incidence of the malignant phase.

The causes of secondary hypertension are (i) renal diseases, (ii) endocrine disorders, (iii) coarctation of the aorta. Renal disease may be bilateral or unilateral. Of the bilateral types, chronic nephritis, chronic pyelonephritis either primary or secondary to calculus or other obstruction, lead nephritis and *periarteritis nodosa* should be mentioned. Unilateral renal disease may be chronic pyelonephritis, hydronephrosis or calculus, or an aberrant renal artery may be present. Marshall (1951) has found a significantly higher incidence of aberrant renal arteries in cases of hypertension, and suggests that hypertension may be causally related to this factor, perhaps because of urinary stasis and infection. Of endocrine causes of hypertension, Cushing's syndrome and phaeochromocytoma may be mentioned.

¹ Read at a meeting of the New South Wales Branch of the British Medical Association on September 25, 1952.

In the separation of the various causes of hypertension, one should pay particular attention to the following points as regards the patient—history, examination and investigations.

When the history is taken, the following should be noted: age and sex, the presence of symptoms directly due to hypertension, psychological traits and environment, previous records of blood pressure estimations, previous urinary symptoms or renal disease, a history of albuminuria, a history of toxæmia of pregnancy, a family history of hypertension.

In the examination of the patient, the blood pressure should be estimated after rest. The condition of the peripheral arteries should be noted, and femoral arteries should be palpated simultaneously with the radial artery. The size of the heart should be noted, and the *fundi oculorum* examined. The patient's exercise tolerance should be estimated, and the urine examined for albumin.

Investigations should be carried out as follows. The maximum specific gravity of the urine after water restriction should be estimated and the urine examined microscopically. An X-ray picture of the chest and an electrocardiogram should be taken. The blood urea content and haemoglobin value should be estimated. Intravenous pyelography should be carried out, together with special tests for phaeochromocytoma.

Treatment.

The main discussion of treatment will deal with hypertension *per se* and in particular essential hypertension. At the end, brief mention only will be made of treatment applicable to certain special types of secondary hypertension. The fact that fashions in the management of hypertension have changed in the past, and are still changing, is adequate proof that the management is on the whole unsatisfactory. After experience in the treatment of hypertension, one feels that the average patient is right when she continues to ask for "my blood pressure tablets, please doctor" (phenobarbitone).

Before one assesses either the necessity for treatment or the expected beneficial results, one must have some idea of the expected prognosis in any given case. There is often a tendency to treat the sphygmomanometer reading rather than the patient. A few broad principles of prognosis will therefore be stated by dividing hypertension into four groups. (i) Labile intermittent or remittent hypertension requires no treatment as it tends to remain benign and symptomless for years. (ii) Sustained uncomplicated hypertension does not require treatment except in subjects aged under forty years. In this group males tend to get cardiac involvement with left ventricular failure and coronary artery disease sooner than females. In a smaller number of subjects the brain and kidneys eventually become affected. Subjects in this group aged over fifty-five years will have their life expectation shortened very little. (iii) In sustained complicated hypertension with symptoms such as severe headaches, dyspnoea, angina, and impaired vision, the diastolic pressure is usually more than 120 millimetres of mercury, and the expectation of life is not likely to be more than three years. (iv) In malignant hypertension, with severe retinal involvement including papilledema, termination is usual within a year from cardio-renal failure or cerebral hemorrhage.

As a guiding principle, hypertensives in groups (i) and (ii) require no specific treatment directed to reduction of the pressure. Those in groups (iii) and (iv) who have not great involvement of organs are those one should select for treatment designed to reduce the blood pressure.

General Treatment.

General treatment should include the following measures: (i) reassurance, with the carrying on of normal life, the rate being moderated only if indicated; (ii) reduction of obesity, with a relatively low calorie intake; (iii) reduction of sodium intake; (iv) moderation in the use of alcohol and tobacco; (v) mild sedation, when indicated, with one of the barbiturates.

Blood Pressure Reduction.

Sympathectomy.—Smithwick is the best known modern advocate of sympathectomy. In his latest paper on the subject, Smithwick (1951) analyses a large series of patients who have had sympathectomy and compares them with a "control" series. He deduces that sympathectomy is the treatment of choice in nearly all cases of essential hypertension, and that the long-term results are good. McMichael (1952) has collected the British figures, and by pooling three series of cases has found that there was a significant fall of blood pressure in only 18% of patients, and this over a relatively short period of observation of about two years. Thus there is considerable difference of opinion regarding the benefit of sympathectomy, but on the whole it appears to be of benefit in the following types of cases: (a) in groups (iii) and (iv) above, provided no severe cardiac, renal or cerebral damage is present and the patient is aged under fifty years; (b) in chronic renal disease, when the blood pressure first starts to rise without renal failure; (c) in hypertension following toxæmia of pregnancy (Chris, 1951); (d) before or during pregnancy in a case of essential hypertension.

Salt Depletion.—Kempner's (1948) rice diet works on the principle of salt depletion and aims at reducing the sodium intake to 200 milligrammes per day. This does reduce the blood pressure, but very few patients will tolerate the diet for long. Ion exchange resins are also being used with a similar object in view.

Ganglion-Blocking Drugs.—The use of ganglion-blocking drugs is the latest form of treatment and aims at producing a "medical sympathectomy". The drug usually used is hexamethonium bromide or bitartrate. The type of patient selected is similar to that for sympathectomy, those in groups (iii) and (iv) above being mainly chosen. This treatment has also been used with benefit in cases of chronic nephritis without much rise in blood urea level, and in toxæmia of pregnancy. On a maintenance basis it may be given orally or subcutaneously. Most are agreed that parenteral administration produces the most efficient results, but there are obvious disadvantages to long-term domiciliary treatment. When the drug is given orally, absorption is incomplete and variable. A large series was reported by Smirk and Alstad (1951), with very encouraging results achieved for periods up to fourteen months. They favour subcutaneous administration three times daily, with some restriction of salt intake as well. More recently McMichael (1952) has advocated similar treatment with doses up to 750 milligrammes given subcutaneously daily. Rosenheim and McMichael (1952) discussed this line of treatment recently at the Royal Society of Medicine. Mackey and Shaw (1951), Murphy (1951) and Blainey (1952) have described fairly satisfactory results, mainly with the use of oral medication, the top doses being eight to ten grammes daily. There have been others who maintain that no beneficial effect at all is produced in the long run with this treatment. One of the disadvantages of this drug is the likelihood of producing uncomfortable side effects. These are mainly due to simultaneous blocking of the parasympathetic nervous system. Paralysis of accommodation, nausea and vomiting, constipation and retention of urine are the common effects. Another difficulty with large doses has been the production of bromism when the bromide salt is used. This is usually characterized by drowsiness, confusion, and in some cases hallucinations. These side effects often prove so troublesome that treatment at an effective level has to be abandoned. We are still in the experimental stage, but it does appear that the methonium salts are worthy of continued use in selected cases, and under strict control. Some of the beneficial effect at least seems to be related to sustained postural hypotension. It is also found that the best results are obtained in patients with placid personalities.

Special Treatment.—Unilateral renal disease, phaeochromocytoma, adrenal cortical tumours, and coarctation of the aorta can in some cases be treated surgically. Not all patients with hypertension due to unilateral renal disease respond to nephrectomy. The most satisfactory patients usually are those with atrophic chronic pyelonephritis or hydronephrosis.

Summary and Conclusions.

In my own experience, I say little or nothing about the hypertension to patients who are not going to be treated specifically for it. I am sure that more psychological harm is caused and less physical benefit produced by mentioning the diagnosis or degree of blood pressure to the patient.

Hypertension having been discovered, one should make every effort, especially on clinical evidence, to establish the cause in the individual case. The type and severity of the hypertension can then be correlated so that prognosis can be assessed and treatment outlined.

It is my practice to treat hypertension as such only in those patients who come into groups (iii) and (iv) outlined above. Those in groups (i) and (ii) no doubt benefit by attention to their psychological make-up and environment.

If specific treatment is to be used, the choice seems to be the administration of hexamethonium salts. I have had little experience with parenteral administration, and this may prove to be the ideal method. My experience with oral administration in a number of cases is that relief of symptoms can be produced in most patients provided the side effects are not too uncomfortable. In a few cases only have I been able to maintain a fall in blood pressure readings.

Sympathectomy seems to have its place at present in the treatment of those patients who cannot be efficiently or satisfactorily treated by hexamethonium salts.

One feels that until more is known about the specific aetiology of hypertension, treatment will remain relatively ineffective.

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THE INFLUENCE OF BARBITURATE ON THE SYMPATHETIC NERVOUS SYSTEM.¹

By E. R. TRETHEWIE,

*Department of Physiology, University of Melbourne,
and the Royal Melbourne Hospital, Melbourne.*

BARBITURATE has been known to inhibit mechanisms generally regarded as of vagal autonomic origin; for example, De Waele (1925) found that barbiturate affected the peripheral part of the inhibiting mechanism of the heart, and Lieb and Mulinos (1929) showed that "Sodium Amytal" impaired the response to vagal stimulation. Wright, Florey and Jennings (1938) showed that barbiturate impaired the response to pelvic nerve stimulation. Trethewie (1942) showed that barbiturate inhibited the release of acetylcholine following vagal stimulation, so

¹This work was aided by a grant from the National Health and Medical Research Council.

that evidently the autonomic depressant effects of barbiturate are due to this mechanism. While barbiturates are considered to affect the sympathetic system by a central hypothalamic effect (Keeser and Keeser, 1935), it was not till recently (Trethewie and Gladwell, 1951, 1952) that evidence was presented of an effect of barbiturate on the peripheral sympathetic system. This was done by showing that the release of adrenaline from the suprarenal medulla, which normally occurs following the injection of large doses of acetylcholine, was inhibited after the injection of pentobarbitone sodium ("Nembutal"). This can be regarded as a blocking of the sympathetic at the peripheral



FIGURE I.

Response of the blood pressure of a vagotomized cat under ether and chloralose anaesthesia. Splanchnic intact (adrenalectomy). At S_1 , splanchnic nerve stimulated for thirty seconds. At N , 70 milligrammes of "Nembutal" injected intravenously slowly between the signals. Interval between panels, forty-five minutes. Time in minutes, details in text.

ganglion. In this paper further studies are described concerning the effect of barbiturates on the sympathetic system in man and animals.

METHOD.

Skin Temperature Studies.

The skin temperature was determined with a thermistor held in a glass holder lightly touching the skin surface. Control estimations were carried out to determine whether the skin temperature varied significantly over a period of some hours under hospital conditions. In one instance a cradle was placed over the bed to keep the clothes off the patient (P_1), and in the other two cases (P_2 and P_3) this was not employed. The clothing was unchanged through-

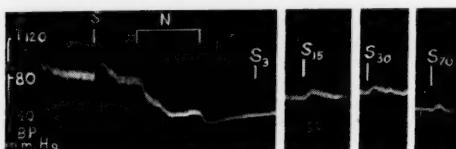


FIGURE II.

Response of the blood pressure of a vagotomized cat under ether and chloralose anaesthesia (adrenalectomy). At S , peripheral end of cut splanchnic nerve stimulated for twenty-five seconds. At N , 70 milligrammes of "Nembutal" injected intravenously slowly between signals. At S_3 , S_{15} , S_{30} and S_{70} , splanchnic nerve stimulated three, fifteen, thirty and seventy minutes after injection, respectively. Time in minutes, details in text.

out the day of the estimation (1.8, 2.5 and 7.0 hour periods), and the patients were kept comfortable in bed, to which they had been confined for the preceding two weeks. Phenobarbital and pentobarbitone sodium were given orally with water.

Basal Metabolic Rate.

The patient arrived fasting at the hospital (having been driven there in a car), and after half an hour's rest lying down the basal metabolic rate was determined at 8.45 a.m. When phenobarbital was taken on the morning of the basal metabolic rate estimation, it was swallowed with one-quarter of a cupful of water two hours before the estimation. Some control basal metabolic rate estimations were carried out with the subject taking

the same amount of water at that time, but no phenobarbital. Fourteen days earlier one of the subjects had taken pentobarbitone sodium ("Nembutal"). Drug medication was given orally: phenobarbital in a dose of 0.06 grammes (one grain) twice one day and once on the following morning, when the basal metabolic rate was taken. "Nembutal" was taken in one dose of 0.18 grammes (three grains) on the morning of the determination only.

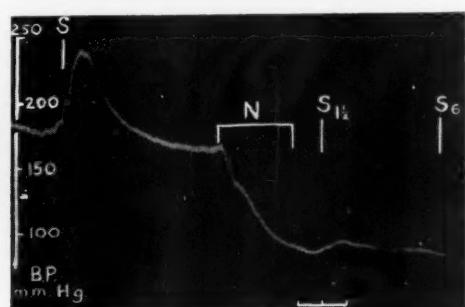


FIGURE III.

Response of the blood pressure of a vagotomized cat under ether and chloralose anaesthesia (adrenal intact). At S , splanchnic nerve stimulated for ten seconds. $S_{1/2}$, one and a half minutes after completion of "Nembutal" injection. S_6 , six minutes after. At N , 70 milligrammes of "Nembutal" injected slowly intravenously. Time in minutes, details in text.

Animal Experiments.

Cats were anaesthetized under chloroform and ether followed by chloralose (which has little effect on the circulatory system), 8.0 millilitres per kilogram of a 1% solution being given intravenously. Artificial respiration was

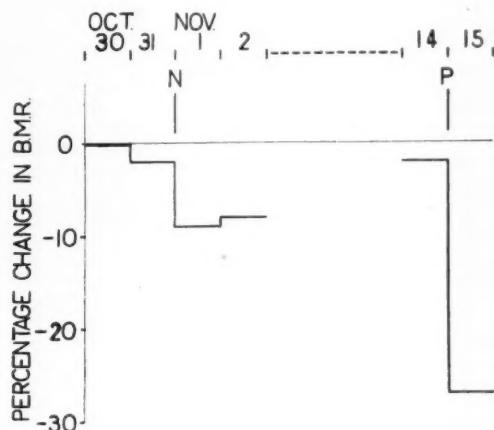


FIGURE IV.

Change in basal metabolic rate in subject P_4 . At N , "Nembutal" taken. At P , phenobarbital taken. Details in text.

given (the volatile ether and chloroform being removed), the vagi were cut, and the splanchnic nerves were exposed below the diaphragm and stimulated from an induction coil.

EXPERIMENTAL INVESTIGATION.

The paper is divided into three sections: (i) direct evidence for depression of peripheral sympathetic responsiveness by animal experiment; (ii) skin temperature changes in man (including hypertensives) produced by the

oral administration of barbiturate; (iii) basal metabolic rate changes produced by barbiturate in man. The varying and interrelated significance of these findings is then discussed.

Peripheral Sympathetic Responsiveness.

(a) *Depression of vasopressor responses to splanchnic nerve stimulation when the suprarenal glands are removed and the splanchnic nerve is intact.*

When the suprarenal glands are removed, stimulation of the splanchnic nerve causes a rise of blood pressure by producing peripheral vasoconstriction. Pentobarbitone sodium will inhibit the effect. This is shown in Figure I at S_1 , where the first two stimulations (for fifteen seconds) produced a rise in blood pressure of 28 millimetres of mercury. At N , 70 milligrammes of pentobarbitone sodium were injected into the femoral vein over a period of four minutes. Three successive stimulations of the sympathetic (S) then produced no rise of pressure till fifteen minutes later, when a rise of six millimetres of mercury only was recorded after fifteen seconds' stimulation. After a further interval of thirty minutes, stimulation again produced a rise of blood pressure of only 12 millimetres of mercury.

(b) *Depression of vasopressor response to splanchnic nerve stimulation when the suprarenal glands are removed and the splanchnic nerve is cut.*

In the absence of the suprarenal glands a similar rise in pressure to peripheral splanchnic nerve stimulation is obtained (as in (a)) when the splanchnic nerve is cut. There is a similar depression to this stimulation when "Nembutal" is injected intravenously. This is shown in Figure II at S_1 , where the first two stimulations (for twenty-five seconds) produced a rise of blood pressure of 20 and 22 millimetres of mercury. After the intravenous administration of 70 milligrammes of "Nembutal" (at N) (3½ minutes) the rise to nerve stimulation was abolished three minutes after the completion of injection (S_2 , Figure II). At fifteen minutes (S_{15}), thirty minutes (S_{30}), seventy minutes (S_{70}), a small rise in blood pressure only was obtained.

(c) *Impairment of response to peripheral splanchnic stimulation when the suprarenal glands are intact (splanchnic cut).*

It has already been shown that the suprarenal gland no longer liberates adrenaline in quantity after stimulation by acetylcholine following the administration of "Nembutal" (Trethewie and Gladwell, 1952). When the gland is intact, both suppression of output of adrenaline and nor-adrenaline by the gland and peripheral neurogenic vasoconstriction are evident. This is shown in Figure III. At S_1 , splanchnic nerve stimulation (for ten seconds) produced a prominent rise of blood pressure of 60 millimetres of mercury. This was abolished after the intravenous injection of "Nembutal", 70 milligrammes, at N . Absence of response is shown at S_{15} and S_{30} , one and a half and six minutes after completion of the injection.

Skin Temperature Changes.

"Thermoregulatory adjustment is a balance established between the effects of the stimulation of heat and cold receptors, and the excitation of the hypothalamic centre by the level of body temperature" (Hardy, 1950). Ordinarily a rise of internal temperature from increased metabolism will produce peripheral vasodilatation from stimulation of the central heat regulatory centre, and a fall will produce peripheral vasoconstriction similarly. This occurs when the environmental temperature is constant. However, the balance is not always maintained in this manner. Assuming this balance to be operative in the reduced metabolism produced by barbiturates (to be demonstrated in the next section), one would then expect, in the absence of any peripheral effect of barbiturate, that there would be peripheral vasoconstriction. If the autonomic pathway from the hypothalamus to the peripheral vessels was blocked, on the other hand, such vasoconstriction could not occur. Further, if there was ganglionic blocking or peripheral depression of the sympathetic system (as is shown to occur in the animal experiments recorded above), then, on the

contrary, one would expect to obtain peripheral vasodilatation, since there is normally sympathetic "tone".

In man we have found, as is recorded below, that peripheral vasodilatation does occur in association with the reduced metabolic rate, and therefore it is likely that ganglionic blocking or peripheral inhibition of the sympathetic system occurs in man. The body temperature falls after the administration of barbiturate, and this may be due to both peripheral vasodilatation and reduced metabolism.

To determine whether peripheral vasoconstriction or dilatation is produced by barbiturate, phenobarbital and pentobarbitone were given to hospital patients.

In Table I is recorded the peripheral skin temperature change in such subjects. P_1 was a patient suffering from hypertension, who had been in bed in hospital for five weeks. (His systolic blood pressure was 180 millimetres of mercury and his diastolic blood pressure 100 millimetres.) The investigation was carried out with the patient wearing a bed-jacket, and there was a cradle over the bed which kept the sheets from contact with the limbs. The skin temperature was recorded four centimetres below the elbow and five centimetres proximal to the wrist in each arm and at a fixed point on the dorsum of the foot, and the readings were repeated ten minutes later. The skin temperature readings showed negligible differences. These were averaged. Then the patient was given 0.12 grammes of phenobarbital orally and 1.8 hours later the skin temperatures were again recorded. In all areas the temperature had risen, on the average 1.8° C. (3.3° F.). These findings are recorded in Table I. Since the same area was recorded for temperature change we can analyse the findings in pairs when the probability is $p < 0.01$, a highly significant result. It is considered that the skin temperature has risen significantly following the administration of barbiturate, unless there is normally a rise in the skin temperature over this period, an aspect which is analysed later.

P_2 (a patient suffering from an old, recovered, mild right hemiplegia and a recent mild left hemiplegia, rheumatic carditis and haemoptysis) similarly showed skin temperature changes. Phenobarbital, 0.12 grammes, was given orally at 10 a.m., and seven hours later the temperature of the skin areas showed a rise averaging 1.1° C. (2° F.) (see Table I). This change in temperature is also significant ($p < 0.05$).

P_3 was a patient who had been in bed for two weeks; the blood pressure was 115 millimetres of mercury, systolic, and 60 millimetres, diastolic, the arterial vessels were thickened and cardiac infarction had occurred earlier. This patient was given 0.18 grammes of "Nembutal" orally, and 2.5 hours later the skin temperature had risen 1.9° C. (3.4° F.) on the average, a significant change ($p < 0.05$).

A control experiment was carried out on a patient who had been in bed for two weeks in hospital after a cardiac infarction. The skin temperature was recorded as before below the elbow, above the wrist and on the dorsum of the foot on the right side. Estimations were made at 11.30 a.m. and 80 and 290 minutes later. Medication for the patient had been with phenobarbital, 0.03 grammes twice a day, at 8 a.m. and 12 midday, and 0.06 grammes at 4 p.m. This amount was taken on the day before the test, and at 8 a.m. 0.03 grammes only was taken on the day of the test and none thereafter till completion of the test. Three and a half hours after this final small dose (nineteen and a half hours after the second last dose) the skin temperature averaged 28.8° C. Eighty minutes later the skin temperature averaged 28.6° C. (a negligible fall of 0.2° C. or 0.3° F.). Two hundred and ninety minutes later again the skin temperature averaged 28.8° C. (equal to the initial figure), there being a slight fall in the temperature of the arm and a slight rise in the temperature of the foot. The mean difference in temperature is so negligible that there is no significant change.

The subjects had all been kept in hospital in a large ward, away from a window or open door, with constant night attire and bedclothes. It perhaps was to be expected that the skin temperature would generally remain constant.

TABLE IA.
Temperature Change Following Oral Administration of Barbiturate.

Patient.	Barbiturate Given and Time Interval.	Right Forearm (Upper).	Right Forearm (Lower).	Left Forearm (Upper).	Left Forearm (Lower).	Right Foot.	Left Foot.	Average.	Probability.
P1	Phenobarbital, 0·12 grammes; 108 minutes.	+1·2° C.	+2·9° C.	+0·7° C.	+1·2° C.	+2·1° C.	+2·6° C.	+1·8° C.	<0·01
P2 ¹	Phenobarbital, 0·12 grammes; 420 minutes.	+2·4° C.	+0·6° C.	+2·2° C.	+0·5° C.	+0·35° C.	+0·6° C.	+1·1° C.	<0·05
P3 ²	"Nembutal", 0·18 grammes; 150 minutes.	+2·8° C.	+2·2° C.	+1·0° C.	+0·5° C.	+2·2° C.	+0·5° C.	+1·0° C.	<0·05

¹ P2 after popliteal block with 2% procaine solution, temperature change right foot +1·1° C. (interval thirty-three minutes); leg, +0·9° C.

² P3, after popliteal block with 2% procaine solution, temperature change left foot -0·1° C. (interval sixteen minutes); leg, -0·2° C.

Effect of Barbiturate on the Basal Metabolic Rate.

In this section evidence is produced to show that phenobarbital and pentobarbitone in therapeutic dosage lower the basal metabolic rate greatly.

Reflex effects associating heat production with heat loss show that usually when the production rises there is peripheral vasodilatation. While this is not always the case, if we are able to show that the basal metabolic rate is

been found to yield very constant figures among those who are submitted for examination on clinical grounds, although it is not unlikely that drug medication in addition to apprehension owing to illness may be causing variation of the baseline. This will be discussed in another paper. Other than obtaining a satisfactory control value, it is important to remember that the pharmacological action of barbiturates on motor activity is remarkably prolonged. Similarly, one may expect a prolonged metabolic rate effect. Also phenobarbital is not so rapidly acting as pentobarbitone.

The findings in subject P₄ are shown in Table II. Two control basal metabolic rate determinations gave the figures 0 and -2%. On the third morning 0·18 grammes of pentobarbitone sodium were taken orally two hours before a

TABLE IB.
Control, Patient 11.

Time Interval.	Right Forearm (Upper).	Right Forearm (Lower).	Right Foot.	Average.
80 minutes	..	-0·15° C.	-0·1° C.	-0·3° C.
290 minutes	..	-0·4° C.	-0·8° C.	+1·1° C.
				+0·18° C.

reduced by barbiturate and in addition in spite of this that peripheral vasodilatation occurs, the probability is, especially when the result is taken in conjunction with the animal experiments described above, that there is a peripheral sympathetic inhibitor effect of barbiturate either post-ganglionic terminal or pre-ganglionic.

In an attempt to determine whether there was reduced heat production in association with peripheral vasodilatation, basal metabolic rate studies were carried out.

TABLE II.

Day.	Basal Metabolic Rate.	
	Control Estimation.	Experimental Estimation.
1	..	0
2	..	-2%
3 ("Nembutal" given)	..	-9%
4	..	-8%
16	-2%	—
17 (Phenobarbital given)	—	-27%

Previous workers have reported an increase in the basal metabolic rate soon after the giving of phenobarbital, but apparently only one determination was made prior to the giving of the drug (Boothby and Rountree, 1923), and the effect was followed for only ninety minutes. Thus the later "B.M.R." was estimated later the same day, so the metabolic rate was not basal. Anderson, Chen and Leake (1936) state that they confirmed this finding for small doses, but an analysis of their findings shows that the change was not significant. Even a large dose (eight milligrammes per kilogram) produced no effect on the metabolic rate, and once more the criticism applies of following the effect this time only for forty minutes.

Cowan (1945) found that when scientific personnel were examined under basal conditions the metabolic rate was remarkably constant. For this reason such personnel were chosen for this investigation. Hospital patients have not

TABLE III.
Effect of Phenobarbital on the Basal Metabolic Rate.

Subject.	Basal Metabolic Rate.	
	Control Estimation.	Experimental Estimation. ¹
P4	(i) 0 (ii) -2% (iii) -2%	-27%
P5	(i) -6% (ii) -8%	-11%
P6	(i) +1% (ii) -8%	-24%
P7	(i) -2% (ii) -3%	-26%

¹ Thirty-six hours after ingestion of phenobarbital, one grain twice a day.

further basal metabolic rate estimation. The subject stated that the marked effects of the drug were wearing off. The basal metabolic rate estimation then was -9% and on the following day -8%. Twelve days later this subject again had a control metabolic rate estimation (-2%) and immediately after that took 0·06 grammes of phenobarbital. That evening a similar dose was taken, and again at 7 a.m. on the following day. The metabolic rate at 8·45 a.m. was -27%. To evaluate the findings in Table II we may compare the normals 0%, -2%, -2% with the experimental -9%, -8%, -27%, and this gives a probability of 0·05. The change in basal metabolic rate is significant statistically. The findings in all the subjects taking phenobarbital are recorded in Table III. Subject P₅ had control basal metabolic rate estimations of -6% and -8%, P₆, +1% and -8%, and P₇, -2% and -3%. The findings after the giving of phenobarbital were -11%, -24% and -26% respectively. On the average, including P₄, the basal metabolic rate was -3·5% before phenobarbital and -22% after phenobarbital. This finding is significant statistically ($p = 0·035$).

This finding is important with regard to the estimation of the basal metabolic rate in thyrotoxicosis and will form the substance of a later paper.

DISCUSSION.

While barbiturate has long been known to inhibit mechanisms generally regarded as of vagal autonomic origin by a peripheral mechanism, the effect of the drug on the sympathetic system has been regarded as a central one. Few will deny that barbiturates form one of the most useful groups of drugs in the management of hypertension in association with other measures. On the one hand, many regard barbiturates as of value as sedatives without reference to specific effects (Evans, 1951). Frew and Rosenheim (1949) presented evidence to suggest a similarity between the effect of barbiturates ("Seconal") and tetraethylammonium bromide (T.E.A.B.) on the diastolic pressure, and concluded that this could be explained by depression of the central autonomic by barbiturate, with the ultimate production of a similar effect to that of T.E.A.B., which is a ganglionic-blocking agent (Acheson and Moe, 1946). If the fluctuations of blood pressure which occur in hypertension are of sympathetic origin, and many consider that they are, a blocking agent has therapeutic importance especially if the fluctuations produce permanent effects on the vessels.

Sympathectomy, of course, has been advocated in certain instances for treatment.

On the other hand, Masserman (1937) was unable to detect any direct effect of barbiturate ("Sodium Amytal") on the hypothalamus except for slight diminution of the vasomotor and respiratory response after stimulation.

It is suggested that the evidence put forward in the present paper satisfactorily explains the favourable therapeutic effectiveness of barbiturate in hypertension, and more fundamentally explains the discrepancy between the contention that barbiturates depress the sympathetic system centrally and the failure of Masserman to confirm this work by direct experiment. We do not discuss here control effects of barbiturates.

It has been shown that there is a block between the pre-ganglionic level and the peripheral level—that is, either at the ganglion or at the peripheral sympathetic ending. In view of the inhibition of the output of adrenaline by the suprarenal (Trethewie and Gladwell, 1952) following the injection of acetylcholine after barbiturate therapy, while the pressor response to adrenaline is little depressed, we suggested that the major blocking is at the ganglion.¹ On the other hand, immediately after injection of barbiturate there is some depression in response to adrenaline, and so we suggested that there is slight peripheral (post-ganglionic) depression also.

The present studies following nerve stimulation show conclusively that in the animal the blockage is certainly peripheral to the cord and in fact involves the sympathetic pathway, and for the reasons outlined above these findings, when taken in conjunction with the metabolic rate and skin temperature changes, indicate that in man also (in hypertensives) there is a similar sympathetic block.

The rationale for the treatment of hypertension with barbiturate drugs (in addition to general management and dietetic measures) is thus placed on a firmer foundation; in fact it produces pharmacologically a similar effect to surgical sympathectomy. T.E.A.B. produces a similar effect, though more powerfully and perhaps more evanescently. The effect of phenobarbital on the basal metabolic rate which has been shown to occur, is also probably of considerable therapeutic value in the treatment of cardiac patients and hypertensives.

SUMMARY.

- Peripheral sympathetic "blockage" by barbiturate has been demonstrated in animal experiment.
- Reduced basal metabolic rate and peripheral vascular dilatation have been shown to occur in human subjects (including hypertensives) after the administration of barbiturate, more particularly phenobarbital.
- The significance of these findings in relation to the treatment of patients with hypertension is discussed.

¹This has been recorded independently in a later paper by Larrabee and Posternak (1952).

ACKNOWLEDGEMENTS.

Thanks are due to Miss Beryl Splatt, of the Royal Melbourne Hospital, for the basal metabolic rate determinations, and grateful acknowledgement is made to Dr. C. H. Fitts for access to patients.

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Reports of Cases.

A CASE OF HODGKIN'S DISEASE WITH SPINAL CORD INVOLVEMENT TREATED BY NITROGEN MUSTARD.

By F. A. E. LAWES AND H. J. HAM,
Sydney.

THE following case is recorded as an example of the dramatic improvement which can follow the administration of nitrogen mustard to a patient suffering from Hodgkin's disease when an immediate result is required.

Nitrogen mustard has been available in Australia during the last few years in the form of the compound methylbis (β -chloroethyl) amine hydrochloride, also known as H_2N , and the clinical use of this was first described by Jacobson and his co-workers.

Nitrogen mustard is a systemic cell poison closely related in its mode of action to total body irradiation. It acts and produces toxic effects more quickly than X rays; but its therapeutic effects may be less prolonged. It is as well to realize that considerable damage to the haematopoietic tissue may result from nitrogen mustard therapy. This treatment does not seem to produce oedema in tissues immediately afterwards, such as has been known to occur after X-ray therapy. In properly selected cases of generalized Hodgkin's disease, and particularly in the treatment of patients in *extremis*, nitrogen mustard therapy may produce dramatic results in a matter of hours. How-

ever, as a routine measure in generalized disease and in the treatment of localized Hodgkin's disease, it is considered preferable to use deep X-ray therapy.

Clinical Record.

A male subject, A.C., aged thirty-one years, was referred to the Royal North Shore Hospital by Dr. E. C. Blomfield, of Bega. He was admitted to hospital on June 26, 1951, complaining of pain and stiffness in the neck and right shoulder, and of weakness of the right arm for the past six weeks. He had been well before this. These symptoms, mild at first, soon became more severe, and a burning pain spread from the neck to the right shoulder, arm, forearm and hand. Also there was tingling in the fingers. The pain was worse at night and was aggravated by the patient's lying on his right side. Maximum comfort was obtained in the supine position. The pain was eased, but not abolished, by heat. At first no cause was found for his symptoms and he was treated for fibrosis, but two weeks before his admission to hospital the pain became acute, particularly on the right side of his neck: it "seemed to paralyse" the whole of his head and neck. Injections of morphine were given to relieve him. At this time swellings in the neck were seen and felt, and he was sent to hospital with a diagnosis of Hodgkin's disease. He noticed that his right arm was weaker than his left.

Examination of the patient revealed stiffness of the neck, so that the head was inclined towards the right shoulder and any movement caused pain. The only abnormalities of the nervous system were diminished muscle power and sensation in the right upper extremity. Enlarged lymph glands were felt on both sides of the neck. On the right side there was one solitary enlarged gland—soft and not attached to the skin and freely movable—and on the left side a similar large gland was felt and several discrete smaller ones, not tender and not attached to the skin. There were no other enlarged glands; the spleen was not palpable and the liver was not enlarged. Examination of a gland which was removed from the right side of the neck revealed the changes of Hodgkin's disease, with numerous, very large, Reed-Sternberg cells. No abnormality was found in any other system.

Nine days after his admission to hospital great weakness and numbness of the right upper extremity were present; also difficulty of micturition was evident. Two days later retention of urine was present, necessitating the use of a catheter. Two days after this he was unable to move any of his four limbs. Spastic paralysis and diminution of sensation of all limbs were noted. The intercostal muscles and diaphragm were similarly paralysed, he was unable to cough, and only the accessory muscles of respiration were in action. The abdominal reflexes were absent. The tendon jerks were exaggerated and bilateral ankle clonus was present. He was unable to lift his head, nor could he turn it from side to side. He was placed in a respirator. Pain was relieved by injections of "Omnopon", 20 milligrams (one-third of a grain). His weight was 60 kilograms.

It was decided to treat him by intravenous injections of nitrogen mustard, with the dose of 0.1 milligramme per kilogram of body weight per day. On the next day he was given an intravenous saline infusion and a dose of six milligrammes of nitrogen mustard was injected into the tube. This dose was repeated on the next three days—four injections in all. After the third injection he was able to move both legs and had recovered some use of his respiratory muscles. After the fourth injection the intercostal muscles were being used and he was removed from the respirator for one hour. On the sixth day after the beginning of the treatment he was removed from the respirator and returned to the ward. He felt well, but had some numbness in the hands and occasional pain in the front of the chest. He was able to cough, and micturition was normal. The limb reflexes were still exaggerated and bilateral ankle clonus was still present. He was anxious about the tightness of the chest and feared a recurrence of paralysis. The glandular enlargement had disappeared, so that palpation of the neck and axillæ revealed no abnormality. All his symptoms gradually subsided and he made an uninterrupted recovery.

Lumbar puncture was not done. At first he was too ill and later was so well that it was not considered necessary.

An X-ray examination of the cervical region of the spine revealed no abnormality, and also an X-ray film of the chest was normal.

When he was admitted to hospital an examination of the blood revealed no anaemia and a leucocyte count of 13,100 per cubic millimetre, 63% being neutrophile cells, 25% lymphocytes, 6% monocytes and 1% eosinophile cells. Ten days after the last injection of nitrogen mustard the white cells numbered only 1600 per cubic millimetre. He was given a transfusion of one litre of whole blood and the leucocyte count rose to 5800 per cubic millimetre in the course of the next eight days.

He was discharged from hospital, symptom free, after a stay of five weeks.

Ten weeks later he was examined again. He was complaining of a recurrence of pain in the neck and right shoulder, not so severe as formerly. No glands were palpable. It was decided to give a course of deep X-ray therapy to the neck. After this all his symptoms subsided. He was again examined on January 9, 1952; he was feeling well and had no pain; no enlarged glands or any other abnormality was detected. He has resumed his work as a motor mechanic.

Comment.

Involvement of the central nervous system in Hodgkin's disease is a well-known, but rare, complication. In 1927 Ginsberg called attention to the paucity of information in text-books of neurology regarding the involvement of the central nervous system in Hodgkin's disease. Winklemann and Moore (1941) reviewed 17 cases of Hodgkin's disease in which the nervous system was implicated, and pointed out the necessity of a careful evaluation of widely distributed neurological signs and symptoms, which may be the earliest indication of Hodgkin's disease. In one of their cases the original diagnosis was "menopausal syndrome"; but the patient was admitted to hospital stuporous and with left-sided paresis. Post-mortem examination revealed bilateral cerebral lesions and epidural spinal masses, and involvement of the brachial plexus. In another case autopsy revealed an epidural mass within the spinal canal adherent to the dura in the thoracic region. The involvement of the central nervous system was held by these writers, after a review of the literature and consideration of their own cases, to be the result of direct extension from adjacent Hodgkin's nodules. The spinal cord is affected by penetration through the intervertebral foramina. The late E. L. Cooper in 1935 reviewed 67 cases of Hodgkin's disease, in one of which paraplegia was the first symptom. Autopsy revealed that Hodgkin's tissue had penetrated through the intervertebral foramina in the lumbar region and within the spinal canal had compressed and displaced the *cauda equina* and *conus medullaris*.

In order to obtain a more lasting effect a course of deep X-ray therapy was given to the neck.

Allen and Mercer (1936) reviewed the literature on spinal symptoms of lymphadenoma.

An interesting report of a patient who died from transverse myelitis complicating Hodgkin's disease is given by Beresford and McLetchie (1948). This patient had a transverse lesion of the spinal cord in the lower dorsal region. All the glandular masses had been controlled for three and a half years. Then glands in the right iliac fossa had become involved and symptoms of paraplegia appeared; but the post-mortem examination, six months later, revealed no trace of lymphadenoma anywhere, and nothing to account for the myelitis.

Our own patient, A.C., evidently had involvement of his brachial plexus by Hodgkin's tissue as the first manifestation of his disease. This was soon followed by a penetrating mass affecting the cervical region of the spinal cord. This case shows that neurological symptoms may be the first symptoms of Hodgkin's disease, that the progress may be rapid, and that nitrogen mustard therapy may be life-saving.

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THE LATE RESULTS OF CHOLEDOCHO-GASTROSTOMY WITH A PERMANENTLY OBSTRUCTED AMPULLA OF VATER.

By F. J. GRAHAM,
Rockdale, New South Wales.

Clinical Record.

MRS. X, aged sixty years, was admitted to hospital on July 24, 1940, suffering from *icterus gravis*. She gave a history of having had jaundice with periodic attacks of gastric pain and the passage of white motions and red urine for some four or five weeks previous to her admission to hospital.

She was placed under medical care for a fortnight, when X-ray examination revealed a diseased gall-bladder. She was then transferred to me for operation. I saw her for the first time on the operating table (August 9, 1940), a spare, deeply jaundiced and emaciated patient. When the abdomen was opened through a paramedian incision the common bile duct presented; I first thought it was small bowel attached to the under-surface of the liver. The liver was somewhat enlarged, as was also the pancreas. The gall-bladder did not appear diseased, but it contained two small stones. The internal organs were literally green. The common duct was easy to palpate in its full length. I could find no stone and hence was loath to open the duct, and I decided to remove the gall-bladder and establish external drainage of bile by inserting a small rubber tube in the cystic duct, hoping thereby to relieve the biliary congestion and perhaps establish normal drainage again. That hope, however, did not eventuate. The patient improved but little in health and the tube was gradually removed over a period of three weeks. A biliary fistula formed, and after three months the patient was removed to a convalescent home with a tentative diagnosis of carcinoma of the head of the pancreas (a biopsy had not been carried out). During that time the patient was confined to bed and the motions remained clay-coloured throughout. Occasionally the fistula closed (five days being the longest period of time), and this caused pain in the right upper quadrant and tenderness on palpation, relief coming only when the fistula discharged again. Finally the fistula closed completely and the patient was transferred to hospital again. She was then in a low state of health, suffering from intense biliræmia, intolerable itching, anorexia and loss of weight, and becoming mentally unstable. I considered her a "poor risk" for operation and I explained her serious condition to her, adding that she might lose her life on the operating table. To this she was reconciled, and she asked me to operate again. As the patient was hourly growing weaker I decided to operate at once, hoping that at least I might reestablish external drainage or, better still, have time to anastomose the common duct to the small intestine.

On opening the abdomen I found the same condition existing as was found at the first operation, except that

there were dense adhesions around the gastro-hepatic omentum, the cystic duct was completely sealed and the common duct was visible through the adhesions.

Whilst dissecting around the duct I accidentally opened it on its medial aspect (just what I hoped to avoid). However, having done so, I extended the lesion to admit my index finger. I was able to reach the ampulla but could find no stone, and it felt as though it was blocked with soft matter of the consistency of lymph tissue or lymph nodes: I tried sounds but failed to reach the bowel. The stomach being in immediate proximity to the choledochus, I quickly decided to anastomose them, using a stab wound in the stomach large enough to correspond with that in the duct, and fashioning the stoma with fine catgut carried on a small bowel needle, using one layer of suture only. The anaesthetic agent was ether given on an open mask. The patient's condition was now grave and we stopped the anaesthetic at this stage, closed the abdomen and placed the patient on her right side on the trolley. I accompanied her to the ward, and on her way there she came out of the anaesthetic and as she was lifted onto her bed she literally swamped it with bile. The patient was given a sedative (morphine) and kept on her right side until vomiting ceased, when she was placed comfortably in the recumbent position with her shoulders slightly raised. She was given fluids to drink and was able to take light nourishment after twenty-four hours. The clay motions quickly disappeared and the urine, which had been a deep mahogany colour, became normal. The patient made an uneventful recovery and left the hospital on the seventeenth day after the operation. Having been confined to bed for some five or six months, she was anxious to go home and, being unable to walk owing to her physical weakness, she was carried to a waiting car. I happened to see the patient as she was leaving, and I remarked to her casually that I should like to see her in six years' time. She must have made a note of the date, for she called at my rooms exactly six years later to the day and introduced herself. She told me that she had enjoyed good health since the operation and had gained two stone in weight. I asked her if she had suffered any discomfort through the operation, and she replied: "No, except for a stitch in my stomach when throwing the washing on the line."

Recently, both at home and abroad, whilst discussing this operation, I found many sceptical of its ultimate success; they held the view that the stoma would not function for long or would most likely become obstructed by the influx of food. These views prompted me to look the patient up again. She is now in her seventy-first year. I found her strong, active and mentally alert, carrying on her household duties, and in addition visiting and attending to the wants of sick people in her locality. She tells me that when she eats much fat she becomes slightly bilious but does not vomit. She finds that a fat-free diet suits her best, and she has not had to consult a doctor since the operation—now more than eleven years ago.

I am indebted to Dr. J. A. Vote and Dr. C. D. Badham, radiologists, for the following report and diagnosis:

As the barium was administered there could be seen a tenting of the lesser curvature of the stomach in its upper half, actually at the junction of upper and middle thirds, and from the apex of this tent barium could be readily observed to flow into the common bile duct. Thus, there exists a patent choledochogastrostomy and the anastomosis was quite freely patent. The barium filled the common duct and a little, I feel sure, flowed through the ampulla of Vater to enter the duodenum. The barium was also seen to flow in retrograde direction along the common bile duct and to enter some of the ramifications of the hepatic duct. There could also be seen a loop of filled barium, the orifice of which is close to the anastomotic site. This loop is lobulated in character and I feel sure is due to the proximal part of the cystic duct and the lobulations are the same as seen in oral cholecystography when the spiral valve of Heister is visualized.

Diagnosis: No abnormality can be detected in the stomach, duodenum, or proximal small bowel. There is anastomosis between stomach and common bile duct. The anastomosis is quite freely patent and the common

duct and hepatic ducts fill with barium, also the proximal portion of the cystic duct. A little of the barium, I feel sure, flows through the ampulla of Vater to enter the duodenum.

The patient experienced no ill effects from the administration of the thin opaque meal.

Discussion.

General practitioners who have resided in the same locality over long periods (myself over thirty-five years) are given opportunities of seeing the beginning and the end of many ailments and diagnoses. We have of necessity, as it were, to live with our patients. Amongst these ailments may be mentioned cancer of the head of the pancreas, chronic pancreatitis, and malignant disease of the gall-bladder. These patients are frequently discharged from hospital with biliary fistulae. So long as the fistula discharge the patients lead a miserable existence, some for many years, relief coming only when the fistula close and death supervenes. Internal drainage might have given some of those patients much relief and freedom from intractable pruritus. It is on record that patients have been known to live for over two years after choledocho-enterostomy when the obstruction in the ampulla was due to malignant disease of the head of the pancreas, the diagnosis having been confirmed at autopsy.

The gall-bladder and bowel are frequently used for effecting internal drainage. The former, however, lends itself to infection and often shrinks with age, and when the bowel is used there is always the chance that septic influx into the common duct may cause cholangitis. If I had used either of the above methods of drainage in the case under review I doubt whether I should have had the same lasting results, and if I had been less conservative at the first operation and carried out the choledocho-gastrostomy then I feel sure I should have had a good result and saved the patient much prolonged distress.

In chronic ampulla obstruction I think the operation of choice is choledocho-gastrostomy. The fact that the duct lies along the lesser curvature of the stomach facilitates the operation and calls for but little derangement of the anatomical structures. The result in the present case refutes the belief that directing the bile into the stomach "can only be makeshift and wholly unphysiological". It is unphysiological; but the patient can adapt herself to the new condition and live comfortably, the bile flowing freely into the stomach through a stoma approximately 1.5 centimetres in diameter.

Reviews.

A Textbook on the Nursing and Diseases of Sick Children:

For Nurses. By various authors, edited by Alan Moncrieff, M.D., F.R.C.P.; Fifth Edition; 1952. London: H. K. Lewis and Company, Limited. 9" x 6", pp. 784, with 161 illustrations. Price: 37s. 6d.

The fifth edition of "A Textbook on the Nursing and Diseases of Sick Children" has appeared five years after the previous one. It is still contributed by various authors, all of whom are members of the staff of the Hospital for Sick Children, Great Ormond Street, London, which ensures that the contents may be related closely to the practice and teaching of that great paediatric centre. The editor is Professor Alan Moncrieff, of the University of London, and we have his assurance that a complete revision has been made for the present edition, which has been brought up to date, rearranged and amplified. New chapters have been included on bacteriology, burns, plastic surgery and other subjects, such as dietetics and infant feeding. These chapters are somewhat uneven, and some of them seem to be unnecessarily elementary and incomplete. The book as a whole is a demonstration of the breadth and depth of the instruction supplied nowadays for nursing trainees, who should surely know a great deal more about dietetics and infant feeding, for example, than they will find in this text-book.

Part II, on diseases of children, is divided into 22 chapters with an admirable appendix. Many of these chapters should

be greatly appreciated by medical students, because of the fundamental presentation in simple language of matter which is dealt with abstrusely in medical text-books; here they will find the gist of it written by experts and specialists who know how to teach hard scientific subjects in everyday language. From that aspect there is nothing better in the book than Mr. Alec Rae's new presentation in the appendix of the *materia medica* and pharmacology. Those sections on drugs and their paediatric application will be of great assistance to all physicians who read them in search of enlightenment and guidance. There are many other outstanding features in this text-book to interest a wider circle than those concerned specifically in the curriculum for nurses.

The Medical Annual: A Year Book of Treatment and Practitioners' Index. Edited by Henry Tidy, K.B.E., M.A., M.D. (Oxon.), F.R.C.P., and A. Rendle Short, M.D., B.S., F.R.C.S.; seventieth year; 1952. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall, Limited. 8½" x 6", pp. 556, with 51 illustrations, a few in colour.

Few people cannot know about "The Medical Annual", but it can be confidently recommended to any newcomers. Entering its seventieth year with the 1952 volume, and still under the editorship of Sir Henry Tidy and Professor A. Rendle Short, it continues to provide a satisfactory means of keeping up to date with current advances, more particularly those with a direct clinical significance. Most fields of medicine and surgery, including the specialties, are dealt with in alphabetically arranged articles by 42 contributors. As usual, certain of the articles are general brief treatises rather than summaries of the most recent literature; an example of this is the article on porphyria. The acceptable custom is maintained of having sections on subjects not usually dealt with in annual review volumes; these include veterinary medicine, occupational health, legal decisions and legislation and geriatrics. Other useful regular features are the list of books of the year, pharmaceutical preparations and surgical appliances.

A Text-Book of Inorganic Pharmaceutical Chemistry. By Charles H. Rogers, Sc.D., Sc.D. (Hon. Univ. Mich.), Taito O. Soine, Ph.D., and Charles O. Wilson, Ph.D.; Fifth Edition; 1952. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson. 9½" x 6½", pp. 850, with 22 illustrations. Price: £5 7s. 6d.

THIS text-book has been written to provide the background knowledge for the inorganic chemical monographs of the United States Pharmacopoeia XIV and National Formulary IX, and as such is mainly of interest to American pharmacists and students. The number of inorganic chemicals used in medicine is, however, decreasing to a core common to every pharmacopoeia, and therefore the book will serve as a useful reference in British countries. Each element is taken in the order in which it appears in the periodic table, and its properties are discussed under the headings of history, occurrence, physical properties, chemical properties, commercial manufacture, official identity tests and pharmacology. The official and important non-official compounds of each element are then dealt with under the same headings. The new edition is modern in approach to complex ion formations, for example, with organo-metallic complexes, and is well supplied with references, mainly, of course, to American literature. There is a short chapter dealing with radioactive substances, and the appendix includes constants for isotonic solution calculations.

Although the authors expressly state that they have not attempted to include quantitative aspects of pharmaceutical chemistry, it is felt that in a book of this nature which covers a restricted field of inorganic chemistry, an attempt should be made to give chemical and physical explanations for the analytical steps in the monographs of the relevant United States Pharmacopoeia chemicals.

Circulatory Dynamics: Physiologic Studies. By Carl J. Wiggers, M.D., Sc.D., F.A.C.P.; 1952. New York: Grune and Stratton. 9" x 6", pp. 108, with 44 illustrations. Price: \$4.00.

"CIRCULATORY DYNAMICS: PHYSIOLOGICAL STUDIES", by Carl J. Wiggers, is the fourth in the series of Modern Medical Monographs. It consists of three lectures which have been published separately elsewhere and which deserved presentation in book form. Ten years ago cardiac catheterization was introduced by Cournand and Ranges, and since that time laboratories throughout the world have been feverishly collecting new data about vascular hemodynamics. The interpretation of these data has led to a rapid advance in

the theory and practice of cardiology, but it demands a training in the physiology of the circulation which the average physician lacks. Those engaged in this work have been looking back more and more to the fundamental studies by Frank, Starling, Wiggers and the later physiologists to assist them in their studies. Wiggers has been engaged in these studies for nearly fifty years and is a unique link between Frank and the present generation. It is therefore fitting that he should present so succinctly the dynamic principles on which modern cardiology now rests. This is a first-rate book; the information it contains is essential to all cardiologists and could be found elsewhere only by patient searching through countless journals. It deserves to be read widely.

The Microbiological Assay of the Vitamin B Complex and Amino Acids. By E. C. Barton-Wright, D.Sc., F.R.I.C.S., 1952. London: Isaac Pitman and Sons, Limited. 9" x 6", pp. 190, with 25 text figures. Price: 27s.

CHEMICAL methods for the estimation of vitamins and amino acids are difficult, generally require much material, and are often not very accurate. During the past ten years microbiological methods have been developed for these estimations which are comparatively simple, very accurate and saving in material. "The Microbiological Assay of the Vitamin B Complex and Amino Acids", by E. C. Barton-Wright, has been written by a master of the subject who, himself, is responsible for much of the advance in technique. This, of course, is a book for the specialist. The descriptions of the methods for the different estimations are beautifully clear and full, but even with these a newcomer in the field would have to spend considerable time and energy before he could be confident of his results. Most of the methods for the estimation of vitamins and all the methods for the estimation of amino acids use lactic acid-producing bacteria. A complex medium is used containing all the requirements in vitamins, amino acids and other things for maximum growth of the lactic bacteria, but lacking in the vitamin or amino acid to be estimated. Graded amounts of the solution containing the substance to be estimated are added to a fixed volume of this medium, and, at the same time, a series is prepared with known amounts of the vitamin or amino acid. After inoculation with the bacteria and incubation for a fixed time the lactic acid produced in the tubes is titrated. Difficulties which may be encountered are discussed fully. Anyone engaged in this type of work will find this book an invaluable guide to procedure.

Essentials of Neurosurgery. By Leslie C. Oliver, F.R.C.S. (England); 1952. London: H. K. Lewis and Company, Limited. 9" x 6", pp. 206, with 50 illustrations. Price: 25s.

LESLIE C. OLIVER has produced an excellent little book on the subject of neurosurgery. For such a subject as neurosurgery, which is highly specialized and is not a very significant part of the curriculum for the undergraduate, one must consider for what readers a book on the subject is written. This book provides very clear information for the undergraduate and for the resident medical officer or other recent graduate. It is not a book for the practising neurosurgeon, although it would be of great value to the resident medical officer on taking up his post as house surgeon in the department of neurosurgery. It should be regarded as a primer to neurosurgery and would, so regarded, be a very useful book indeed.

Properly speaking, the essentials of neurosurgery are surgery and neurology. This book does not approach the subject from that point of view, but discusses rather the procedures employed in neurosurgery and the type of cases dealt with. It would be better to call it a primer than "essentials".

The matter is presented well, and the illustrations are well chosen and helpful. Too much is crammed into the earlier chapters about the clinical aspect of neurosurgical cases; so that probably the uninformed will not gain much from these chapters, and they will be clearly comprehended only by those who are already familiar with the matter discussed. However, Oliver is to be congratulated on producing a book of this size and usefulness upon a subject in which the student has always had great difficulty in finding a text to study. It can be recommended to students and resident medical officers. It would be desirable in a book in which X-ray films are illustrated to show them as they are seen in medical practice instead of publishing positive plates in which the bone shadows are shown in black. A technical

step in printing may be saved thereby and so an economy effected, but if one seeks to produce a book for the guidance of medical practitioners one should not introduce a variation from ordinary experience in this way.

Biochemistry and Human Metabolism. By Burnham S. Walker, M.D., Ph.D., William C. Boyd, Ph.D., and Isaac Asimov, Ph.D., with a foreword by John T. Edsall, M.D.; 1952. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" x 6", pp. 820, with 21 text figures. Price: 96s. 9d.

IT is interesting to find a text-book for medical students on a scientific subject with an entirely new approach. This is found in "Biochemistry and Human Metabolism" by three teachers of the Boston University School of Medicine, B. S. Walker, W. C. Boyd and I. Asimov. The book differs notably from other text-books on biochemistry in the order of presentation of subjects, the relative space allotted to various parts and the choice of subjects treated. The first section deals with proteins and amino acids; while there is much that is good in this, the authors assume in the student a knowledge of physical chemistry which is certainly beyond that of most medical students, and yet they give five pages to a discussion on hydrogen ion concentration in the middle of the discussion on the properties of proteins. Nearly 86 pages are given to the proteins, and while much of it would be of use to an advanced student, much of it is beyond the requirements of medical students. The sections on carbohydrates and lipids are more conventional. There is a long discussion on high energy phosphate bonds before there has been anything on metabolism and enzyme action in general.

Multiple authorship and not very careful editing are shown by lack of correlation of various parts. Thus porphyrin chemistry is discussed in connexion with haemoglobin and again much further on in the book, in connexion with bile pigments, and the treatments are quite different.

Some of the subjects treated seem out of place in a text-book for students beginning the subject. For example, 20 pages are given to the biochemistry of cancer. Nearly 40 pages on reproduction and heredity, interesting though they are, seem out of place in a text-book on biochemistry. There are many other things one could take exception to.

There is a great deal that is very good in the book, but as a text-book for medical students it cannot be considered suitable. The book could be read with advantage after a good course in biochemistry.

Pharmacology, Materia Medica and Therapeutics. By B. N. Ghosh, F.R.P.S. (Glas.), F.R.S. (Edin.); Nineteenth Edition; 1952. Calcutta: Hilton and Company and Scientific Publishing Company. 9" x 5½", pp. 875, with 43 illustrations. Price: 30s.

THE nineteenth edition of Ghosh's "Materia Medica and Therapeutics" comes at a time when a wide diversity of text-books in this field are being published. This book differs from most others in that it forms a detailed compilation of all the essentials of the *materia medica* together with the more applied aspects of pharmacology and an outline of relevant therapeutics. The subject matter is discussed in seven parts, the first and last of which deal with pharmaceutical preparations, standards and processes. Parts II and III are devoted to the administration of drugs and detailed descriptions of pharmacology and therapeutics, while Part IV comprises an account of vaccine and serum therapeutics. The remaining two sections are devoted to radiation therapy and a description of drugs indigenous to India.

The book is thoroughly up to date in the material included, and there are monographs on the newer antibiotics, adrenocorticotropic hormone and the drugs to be found in the 1951 Addendum to the 1948 British Pharmacopoeia. There are also descriptions of several drugs which have outlived their value in therapeutics, and their inclusion would seem to have little justification, especially in a book so essentially practical. For a more complete or handier reference book for the practitioner and student one would need to search very thoroughly indeed; in fact this book can best be compared with "Martindale" in its scope and contents, with the addition of more pharmacology and therapeutics and the deletion of some chemistry. With the current spate of textbooks of pharmacology, frequently enjoyably readable and widely annotated, the need for a concise dictionary of *materia medica* still exists, and the present book is well suited to fill the gap.

The production of this book is not particularly attractive, but it must certainly be the least expensive book of reference

in this subject today. The author, Dr. B. N. Ghosh, is to be congratulated upon the painstaking thoroughness of his compilation and upon the publication of a very useful book.

Sodium Metabolism in Health and Disease. By Douglas A. K. Black, M.D., M.R.C.P.; 1952. Oxford: Blackwell Scientific Publications. 9" x 6", pp. 90, with four text figures. Price: 9s. 6d.

For some years there has been increasing interest in the metabolism of inorganic ions in the body and the effects of disturbances of their metabolism. "Sodium Metabolism in Health and Disease", by Douglas A. K. Black, is a more or less critical summary of available knowledge on the metabolism of a single element. It is a monograph of some 70 pages and was written in competition for the Rogers Prize of the University of London, 1951. The first half of the book gives a short review of the distribution of sodium in the human body, and its regulation by intake, loss by sweat and renal secretion. This is, on the whole, a satisfactory account, but some of the data on "renal handling of sodium" are not very critically considered. The second half of the book deals with abnormalities of sodium metabolism, and the four syndromes of disordered sodium metabolism in relation to body water are considered in some detail. This represents a workmanlike summary of what previous writers have written, but does not materially add to our knowledge.

Taken as a whole, this monograph will be useful to anyone who wishes to know what has been written on sodium metabolism up to the end of 1950. Printing mistakes are much too common for a book of this size.

Modern Practice in Tuberculosis. Edited by T. Holmes Sellors, M.A., D.M., M.Ch., F.R.C.S., and J. L. Livingstone, M.D., F.R.C.P.; 1952. London: Butterworth and Company (Publishers), Limited. In two volumes. 10" x 7", pp. 978, with 263 illustrations, a few in colour. Price: £10 10s.

SINCE the war, there have been two outstanding books on tuberculosis, written in the English language, one by Rich and the other by the late Max Pinner. It is therefore very pleasing to welcome a third, this time a product of Britain.

"Modern Practice in Tuberculosis", ably edited by Sellors and Livingstone, gives the latest views on tuberculosis of all parts of the body. There are nearly forty contributors. All have handled their respective sections capably, some, of course, more brilliantly than others; but the whole is so well balanced and edited that the two volumes give concisely the latest views of every aspect of tuberculosis.

Amongst the outstanding chapters the following merit special mention. (i) The chapter on planning of long-term treatment, by Houghton, in which the author stresses the importance of all workers, physicians, surgeons, nurses, almoners, rehabilitation officers, working together. (ii) That on rehabilitation, by MacPhail, perhaps the shortest and in some ways the most delightful chapter of all. In this, MacPhail stresses the importance for those working in clinics of absolute continuity of care for and interest in their patients from the moment of diagnosis right through to complete rehabilitation. (iii) That on the minimal lesion, by Fowler, in which the author emphasizes the fact that many such lesions developing under observation may have a bad prognosis; he advocates early collapse treatment, but says little of streptomycin. (iv) That on the psychology of the tuberculous patient, by Wittkower. The methods of handling patients when their illness is first diagnosed are well discussed. The author points out that when the diagnosis of tuberculosis is first made and is disbelieved, a period of "doctor shopping" may ensue, during which the doctor who is the least ethical is the one that is most popular with the patient". (v) That on the simple forms of collapse treatment including artificial pneumothorax and pneumoperitoneum, by Livingstone, who is of the opinion that despite the recognized dangers of pneumothorax, this form of collapse is still the ideal one. The pronounced swing against the employment of this form of treatment has, of course, been caused by the dreaded complications of empyema and the unexpanded lung. Livingstone discusses in able fashion the reasons why these mishaps occur and how they can be avoided, so that this therapeutic weapon is rendered so much less hazardous. He suggests that the method of cavity closure is much more likely to be by blocking of the draining bronchus than by fully opening it. This method of cavity closure is not devoid of risk and in surgical circles would cause considerable anxiety at least. An interesting point is that he favours three and a half to four and a half years' duration for artificial pneumothorax.

(vi) That on thoracoplasty, by Sir Clement Price Thomas, who advocates a stable blood sedimentation rate before the operation. He states that the number of ribs to be removed should be estimated, and no departure from the original estimation should be made. He advises removal of a small number of ribs at one sitting to avoid paradoxical movement of the lung. Since 1935 he has the remarkable result of 90% of his patients living with "sputum conversion". Including all those who have died, 60% of his patients obtained "sputum conversion". (vii) That on excision of the lung, by Holmes Sellors, who considers that this form of treatment should be reserved for those cases in which collapse therapy and conservative measures would not be likely to give satisfactory results. In common with Price Thomas, he favours thoracoplasty for upper lobe lesions, unless atelectasis has occurred. But it might well be asked how many cases of pulmonary tuberculosis occur in which there is not some degree of atelectasis, lobular, segmental or lobar, the result of endobronchial disease. (viii) That on tuberculosis of bones and joints, by Griffiths, which is an excellent chapter. The author is most pessimistic about the future of tuberculosis. He states that there has been no diminution in the morbidity of "orthopaedic" tuberculosis in England since 1925 and attributes this to the lack of cooperation between chest physicians and orthopaedic surgeons. Then he expresses the opinion that from a world point of view the outlook is almost too foreboding to contemplate. There is, of course, no room for complacency amongst tuberculosis workers, particularly when the magnitude of the problem, say in India and the Far East, is simply unknown. Yet his criticism seems to be unfair in the light of the excellent control of all forms of tuberculosis in Scandinavia and Canada. In some parts of Australia the criticism is at present justified. But on the credit side it must be remembered that the World Health Organization has at least not been unmindful of tuberculosis as a global problem.

In this review it is quite impossible to cover all aspects. In the first edition there are, of course, a few minor omissions and errata, which will, no doubt, be corrected in future editions. It is suggested, however, that in the chapter by Hugh Reid, the German and French passages should be either accompanied by a translation or given translated. Such passages are irritating to a reader who does not know German, for example; and after all, the work is written in English. It is a matter of considerable interest in these days of increasing thoracic surgical adventures to note that the greatest conservatism has been shown by the surgeons entrusted mainly with the surgical problems. They, too, have emphasized the importance of general medical conservatism and the part played by all workers. Totaling 796 pages, in two volumes on art paper with excellent illustrations and reproductions of many skiagrams, this book should be in the library of all chest physicians and surgeons and should be available as an excellent reference book for all general practitioners.

Principles and Practice of Anesthesiology. By Vincent J. Collins, M.D.; 1952. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9" x 6", pp. 528, with 99 illustrations. Price: £5 7s. 6d.

"PRINCIPLES AND PRACTICE OF ANESTHESIOLOGY", as the name immediately suggests, is a new American publication. The author is Vincent J. Collins, M.D., director of the department of Anesthesiology at St. Vincent's Hospital in the City of New York. The book is published by Lea and Febiger and conforms to the best standard of this firm, the paper, type and general presentation being all that could be wished for. Collins would appear to have written this work as a text-book for students presenting themselves for the examinations conducted by the American College of Anesthesiologists. The field of information has expanded vastly since the earlier texts on the subject, and now in this book covers every possible responsibility of the modern anaesthetist.

A detailed account of the whole work is impossible, but a short summary of one chapter will explain the method used throughout to present the utmost information in the shortest, clearest way. The chapter relating to intravenous use of procaine opens with a brief historical survey. Then follows a list of 24 of the recognized uses of the drug. Pharmacology is dealt with under the headings of chemistry, fate and excretion, and properties. These last, being those of the tertiary ammonium group of nitrogenous compounds, are listed under four headings and each is explained in a separate paragraph. The other headings for the chapter are physiopathology, dosage and technique of administration, and responses and toxicity. This quite full information is very briefly expressed and covers only three pages of the

book. It might appear inadequate, but it provides an excellent summary; and for him who wishes to delve deeper or check the facts, no less than 30 references are quoted at the end of the chapter.

There are 64 chapters. Each covers a separate subject, and much new knowledge is presented which has not previously been collected and published in book form. Such chapters as those on "The Physiology of Posture", "Temperature Regulation and Heat Problems", "The Management of Patients in Coma", "Blood Transfusion", "Inhalation Therapy Principles" and "Inhalational Therapy Technics" offer knowledge about a variety of problems confronting the anaesthetist.

The quoted authority for statements is so complete that the reader can find little with which he does not heartily concur. For instance, the old controversy regarding the relative values of oxygen and carbon dioxide in resuscitation is dealt with thus: "It is unanimously agreed among all workers that oxygen is the gas that must be supplied in carrying out artificial respiration. There is nearly complete agreement that carbon dioxide should generally not be used, and to this effect a joint statement has been issued by the Council on Physical Medicine and the American National Red Cross."

It might be thought that such a condensed collection of facts would tend to make rather dull reading, but quite the reverse seems to be the case. Collins writes clearly and without any padding whatever, yet with a certain charm. The impression created by his presentation is that the knowledge is collated and offered to the reader without any suggestion of cocksureness or aggressiveness.

Comparisons are generally in poor taste, but in this case, it could be said with a measure of confidence that the anaesthetist has not been offered a more comprehensive or easily readable presentation of the knowledge and art of his specialty. The extensive bibliography is possibly one of the most striking features of the book. The references are very numerous, and are most meticulously detailed, providing both food for endless further study and complete authenticity for statements made.

CIBA Foundation Colloquia on Endocrinology: Steroid Metabolism and Estimation. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., assisted by Margaret P. Cameron, M.A., A.B.L.S.; Volume II; 1952. London: J. and A. Churchill, Limited. 8" x 5½", pp. 444, with 96 illustrations. Price: 35s.

SINCE 1949 the CIBA Foundation has sponsored a series of international symposia on endocrinology attended by outstanding workers from many countries. The papers and discussions are being published in a series of volumes. Volume I was recently reviewed in these columns. Volume II contains the proceedings of two conferences on closely related subjects. The first part of the volume, on estimation of steroid hormones, covers chiefly the determination of urinary metabolites of progesterone, oestrogens and corticosteroids. It consists of 22 papers with accompanying discussion and the chairman's closing remarks. The papers deal in detail with the various methods which have been found useful in the separation and estimation of urinary steroids and are, of course, highly technical, but invaluable to anyone interested in this class of investigation. The second part is concerned with the metabolic breakdown of steroids. It consists of 16 papers with discussions. These are very highly specialized chemical discussions, which can be of interest only to advanced workers in the field of steroid chemistry.

As the authors of the papers are among the most distinguished workers on steroid chemistry, one can be sure that they represent the best information available on the subject. It is not a book for general reading.

Notes on Books, Current Journals and New Appliances.

Toward Manhood. By Herman N. Bundesen, M.D.; 1952. London: Harvey and Blythe, Limited. 8" x 5½", pp. 176, with two illustrations. Price: 10s.

In the preface to his book "Toward Manhood", Herman N. Bundesen states that the book is an attempt to lay before boys the whole subject of sex and the part it plays in life, as frankly, as truthfully and as completely as it is in his power to do. The result is particularly happy. With

a good deal of common sense and sympathy, and without undue sentimentality, Dr. Bundesen supplies information and counsel on sex and its importance as well as its problems that should be acceptable to any ordinary lad. He quite reasonably assumes a certain amount of knowledge. He treats his young readers as having some common sense, a fact that should help to gain their confidence. The book is interestingly written and should fulfil its purpose well.

Physician's Handbook. By Marcus A. Krupp, M.D., Norman J. Sweet, M.D., Ernest Jawetz, Ph.D., M.D., and Charles D. Armstrong, M.D.; Seventh Edition; 1952. Los Altos, California: University Medical Publishers. 7½" x 4½", pp. 384, with about 40 text figures. Price: \$2.50.

THE object of the "Physician's Handbook", which is now in its seventh edition, is to provide a readily available source of factual data, laboratory procedures, and clinical aids repeatedly used in all branches of medicine. A remarkable amount of information has been packed into this pocket-sized volume. It is necessarily dogmatic in places and makes no pretence at literary style. However, the information is set out clearly, and the method of indexing makes it readily accessible. It can be recommended to all clinicians, and especially to resident medical officers, general practitioners and physicians.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Progress in Fundamental Medicine", by Paul Cannon, J. A. Cunningham, Klemperer, Albert Kligman, G. K. Mallory, Tracy B. Mallory, J. C. Paterson, L. B. Stoddard, W. Kenneth Cuyler and J. P. Wyatt; edited by J. F. A. McManus; 1952. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 10½" x 7¾", pp. 316, with 74 illustrations and two plates in colour. Price: 96s. 9d.

Consists of "authoritative discussions" of topics of current clinical and pathological importance.

"Manual of Gynaecology", by E. Stewart Taylor, M.D.; 1952. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9½" x 6½", pp. 204, with 70 illustrations. Price: 48s. 6d.

The author states that he has tried to present the basic essentials of gynaecology. Technical aspects of operative gynaecology have not been included, but medical, psychosomatic and endocrinological aspects of diagnosis and treatment have been emphasized.

"A Laboratory Manual of Physiological Chemistry", by D. Wright Wilson; Seventh Edition; 1952. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9½" x 6½", pp. 294. Price: 35s.

Intended for use as a teaching manual and not as a comprehensive reference book.

"Symptoms and Signs in Clinical Medicine: An Introduction to Medical Diagnosis", by E. Noble Chamberlain, M.D., M.Sc., F.R.C.P.; Fifth Edition; 1952. Bristol: John Wright and Sons, Limited. 9" x 6", pp. 488, with 354 illustrations, 19 in colour. Price: 35s.

The fourth edition was published in 1947.

"The Preparation and Writing of Medical Papers for Publication", by W. R. Bett, M.R.C.S., L.R.C.P., F.R.S.L. London: Menley and James, Limited. 7½" x 5", pp. 24.

Based on lectures given by the author in various parts of England, will be supplied gratis on application to the publishers, 123 Coldharbour Lane, London, S.E.3.

"The Pocket Prescriber and Guide to Prescription Writing", by Alastair G. Cruikshank, F.R.C.P.E.; Fifteenth Edition; 1952. Edinburgh and London: E. and S. Livingstone, Limited. 4½" x 3", pp. 310. Price: 5s.

First published in 1882 and intended to assist young doctors "to prescribe from the B.P. or B.P.C. and restrict as far as possible the use of proprietary drugs to ethical preparations that have not yet become official".

The Medical Journal of Australia

SATURDAY, JANUARY 24, 1953.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

"COURAGE, GENEROSITY AND HUMILITY."

THE Christmas broadcast of Her Majesty Queen Elizabeth II, characterized as it was by warmth of feeling and obvious sincerity, must have made an instant appeal to every one of her subjects who heard it. There is no doubt that, as her father and her grandfather did before her, she will in her person maintain the link which binds together the several parts of the British Commonwealth. She told us all, with a belief in the old traditions and in the "courageous spirit of adventure", to set out to build a truer knowledge of ourselves and of our fellow men and to work for tolerance and understanding among the nations. We were to do these things with courage, with generosity and with humility. There is no member of the medical profession in Australia who does not believe in the value of family life—doctors have families of their own and they work among families, especially when they are engaged in general practice. They also claim and would contend stoutly for their membership of a family of medicine, a family of ancient tradition and noble achievement. The Queen appealed to us first of all as members of individual families and then as members of the family of the British Commonwealth. Her words may be heeded by the family of medicine, which extends throughout the British Commonwealth of Nations and beyond it. We may then reflect what the words courage, generosity and humility imply in our own sphere.

Of courage we have read much and it has been discussed more than once in these columns. We think of the courage of "deeds that won the Empire", of valour displayed by men and women in war and industry. These are for all to know and read about. But courage abounds and no medical practitioner can work for long among his patients without finding courage, often of the most superb kind which beggars description, and sometimes where he least expects to find it, courage not only in the presence of pain and disease, but in adversity of all kinds. When he

does not expect to find this rare quality and has it displayed to him, it is probable that he has had no chance, or has not tried, to learn the moral worth or capacity of the person concerned. We speak of physical and moral courage, but most courage has a moral basis, that is to say, it is conditioned by early training and upbringing, by the possession of a philosophy of life, or by a sense of values. Courage may result from a desire for self-preservation in the face of danger and we can imagine mass courage arising in the same way as mass hysteria. The possession of courage implies the absence of fear, or at least that fear has been put into the background. Most men have fear. They may overcome their fear and if they do the display of courage by them is not so difficult. On the other hand, they may be able to push fear aside so that, whatever they do, it comes crowding back onto them, hampering effort and calling for constantly recurring conflict. The man of this second kind who displays courage is much more to be admired than his fearless brother.

We must not mistake bravado for courage; it is like base metal to the golden sovereign. The courage that we should seek is allied to freedom of the spirit; it cannot be imposed on man, it must arise within him because of his own free nature. Courage will help a man, standing alone if need be, to advocate certain action in the face of opposition and even to take it alone, if he is convinced of the rightness of his cause and no other way appears to be open to him. The reference in this instance is to intra-professional matters and relationships. But there is a right way and there is a wrong way of standing alone in advocacy or in action, and it is here that we must introduce the other two qualities named by our Queen, generosity and humility.

Generosity is an attribute commonly thought to be a mark of the physician. Robert Louis Stevenson wrote of the physician: "Generosity he has, such as is possible to those who practise an art, never to those who drive a trade. . . ." But we must not take too much unctuous to our souls. The discretion of a physician may, as Stevenson tells us, be tested by a hundred secrets, and his tact may be tried by a thousand embarrassments; but this is in the nature of his calling, and it means that he has far more opportunities to be generous than other men have. That he so often takes them is to his credit and we must remember that his debt of generosity grows with his increasing opportunities. It has been said that the truly generous is the truly wise. But this carries with it the implication that with the display of generosity there goes a hope of reward—an idea which would be wholly repugnant to members of the medical profession. Some people of course are generous with what does not belong to them, and this cannot be said of medical men and women. When doctors are generous to their patients, they give of their skill, their time and their physical and mental energy. There is another kind of generosity which is possibly of more importance than any other and this is generosity of mind. It was probably this that Her Majesty meant when she asked us to build a truer knowledge of ourselves and our fellow men and to work for tolerance and understanding among the nations. Without it no international tolerance or understanding is possible. But we are thinking of the family of medicine

and of our intraprofessional relationships. Here generous minds are needed; fortunately they are by no means uncommonly found. In their absence courage becomes selfish aggression, and this is quite clear to all beholders. To acknowledge the sincerity of those who differ from ourselves in matters of great import, is just as important as ability to put our own case. When members of one family such as the family of medicine deal with matters of moment, selfish aggression is senseless and can do nothing but harm to the whole family. And this brings us to humility. In the present instance humility is best defined in the terms of Saint Paul's words to the Romans: "I say . . . to every man that is among you, not to think of himself more highly than he ought to think." This means that each of us must know his own ability—and also his own limitations. We have ability that we may use it. Humility may be overdone. The Germans have a proverb: "*Zu viel Demut ist Hochmut*" (too much humility is pride). This is worthy of serious thought. The general conclusion is that if as medical men and women we work together in the family of medicine with courage, generosity and humility, we shall promote tolerance and understanding in the family of medicine, and through this family, as Her Majesty has asked us to do, among the nations of the earth.

Current Comment.

SURGICAL DECISIONS IN THE PRACTICE OF PSYCHIATRY.

MUCH has been written lately about frontal leucotomy as a therapeutic measure of relief in psychiatric disorders, and some of the less technical of these writings indicate that the responsibilities of doctors in this respect are to be increased. The great publicity given to this method is perhaps due in part to the hold on the public imagination which is exercised by its more or less spectacular nature. A method such as the induction of coma by the use of insulin receives much less attention, although it is also a disruptive method so far as cerebral function is concerned; but it should be remembered that leucotomy has this important difference, that it is irreversible. P. Macdonald Tow, working in the Nuffield Department of Surgery at Oxford, has made a good summing-up in an address which he entitles "Therapeutic Trauma of the Brain".¹ He uses first the historical method, and then the physiological, and in arriving at a judgement applies pragmatic tests. It is interesting to be reminded that Hippocrates wrote that the brain was the seat of madness and fears and frights, and that "it is there where lies the cause of insomnia and sleep-walking, of thoughts that will not come, forgotten duties, and eccentricities". Tow then proceeds to modern days, quoting the work of Moniz, who caught the current surgical interest, and started a wave of enthusiasm which has been a good deal modified since. He then turns to physiology, and asks where the trauma is, apart from the deliberate and inevitable operative damage. Just before the last World War Rylander published a study on the effects of removal of frontal lobes in the course of operations for the extirpation of cerebral tumours. This work seems to have been somewhat overshadowed by observations on psychiatric patients, often made, as Tow points out, under conditions not good for calm appraisal. Tow further states that there is now no doubt that leucotomy is a therapeutic procedure, and that it gives considerable relief in "intolerable mental illness". The question he raises is, however, not how much good it does, but how much harm. This

too, has been well canvassed in the literature, but the query cannot well be answered in the environment of the advanced sufferers from schizophrenia; it must also be raised in the patient's social environment. In order to be able to judge whether or not a patient is a fit subject for leucotomy there are many aspects to be considered. The need for a pragmatic test in the treatment of patients with severe or continued psychiatric disorders has been also powerfully stressed by E. B. Strauss in his Croonian Lectures for 1952.² He mentions particularly the need for such an approach in evaluating the results of orthodox psychoanalysis, and points out how disappointingly small are the numbers of successful results. In these lectures he makes clear the desirability of applying the law of causality in psychological medicine, and remarks that the physical methods of treatment now employed in psychiatry are not rational, but empirical. Where they fit in the categories of reason and unreason is plain, but Strauss would not condemn those empirical gifts which occasionally fall into the researcher's hand, such as the Wassermann test, which, as we know, was based at first on false premises. Strauss would have more philosophy as a basis, and warns us that logic *per se* is not enough, for it may not distinguish between reason and unreason. Incidentally he prophesies that leucotomy will yet be relegated to "the museum of grim, outmoded neurosurgical curiosities, even though the procedure is justifiable today in certain cases". Tow finally returns to the warring claims of ethics and usefulness in deciding whether leucotomy should be performed or not, and states that there should be two main indications. These are the restriction of the procedure in its major form to very severely affected subjects, in whom the therapeutic gain is obvious, and the trial and adequate appraisal of lesser ablations of frontal tissue carried out by skilled hands. It is in cases of the second type that the need for ethical caution will be greatest, for the patient who has been able after a fashion to live in mutual tolerance with his social environment before operation may be himself pleased, but his temperamental alterations may create even more trying conditions for others afterwards. It would seem that professional responsibility will be exercised with great care in these problems, and public needs will best be served by careful judgement based on scientific methods so far as these are possible.

SEASICKNESS.

SEASICKNESS can present a considerable problem to the armed services at times, particularly under certain combat conditions. Hence the services have taken the lead in seeking a remedy. A recent report based on a cooperative study by the United States Army, Navy and Air Force will be of general interest. In it H. I. Chinn, S. W. Handford, T. E. Cone and P. K. Smith² discuss the effectiveness of various drugs. They state that antihistamine drugs are not effective on account of their antihistamine action, but "Dramamine" (dimenhydrinate), "Benadryl" and "Perazil" are effective, probably owing to their anticholinergic effects. Scopolamine (hyoscine) and "Artane" act in the same way. In the particular investigation reported a great number of new drugs were tried. "Diatrin" was not effective. "Benadryl", "Lergigan", "Trimeton", and a "Benadryl"-scopolamine mixture were effective. "Scopodex" (scopolamine aminoxyde hydrobromide) gave rise to the worst side effects, including mania. It was found in this intense study that a number of drugs diminished the effects of seasickness, but that side effects were numerous with nearly all the drugs used after a few doses. Drowsiness, insomnia, blurred vision, dry mouth, tinnitus and headache seem to have occurred in a very large number of the persons tested. Even among the untreated controls 41% complained of drowsiness, 24% of insomnia, 32% of dry mouth, and 41% of headache. The subjects were American troops. The results seem to indicate that if you ask a person to tell you his complaints during a sea voyage

¹ *The Lancet*, July 5 and 12, 1952.

² *The American Journal of Medicine*, April, 1952.

(as at other times) you will find that very few have a happy, carefree life. In fact, the psychological factors of suggestion and inaction are much too apparent in this investigation, which was carried out on young soldiers who had nothing to do and who were asked systematically how many of the complaints mentioned they suffered from. Unless American soldiers are different from other soldiers, some such answers as those recorded might have been anticipated. On the other hand, the results may be entirely reliable. In summary, treatment with one or other of the drugs mentioned appears to have lessened the incidence of vomiting. "Benadryl" and scopolamine have been reported as effective in preventing airsickness and seasickness. Scopolamine, in the past, has been found effective without "Benadryl". Phenobarbital, atropine and strychnine combined are also effective, but these are old-fashioned. There seem to be too many prophylactic remedies of seasickness. It is a pity the number could not be reduced to one or two.

BILATERAL ADRENALECTOMY IN MALIGNANT HYPERTENSION AND CHRONIC NEPHRITIS.

A PRELIMINARY REPORT on a surgical and clinical study which is of the first order of importance has been published by J. H. Harrison, G. W. Thorn and M. G. Criscitiello.¹ It is pointed out in the report that until the development of replacement substances such as cortisone, desoxycorticosterone acetate and whole adrenal cortical extract, it was impossible to apply the principle of total removal of adrenal influence, but now it is possible with some degree of safety. The primary impulse for this particular study at Harvard in Boston, Massachusetts, was the experience of one of the authors, who had two hypertensive patients who subsequently developed Addison's disease and became normotensive. When one of these patients was given DOCA in ample dosage, he became hypertensive again. Minimal dosage of this replacement substance allowed a return to the normotensive state. Now, as Harrison, Thorn and Criscitiello go on to state, the necessity of and benefit from the salt-free diet in the management of hypertension are well recognized, and the sodium-retaining effects of DOCA are also well known. Therefore, they planned by total adrenalectomy to eliminate as far as possible the salt-retaining hypertensive factors of the desoxycorticosterone-like substances which are elaborated by the adrenals, and to attempt to modify the cortisone-DOCA substitution ratio thereafter for the individual patient, in proportions compatible with a slightly active existence, at the same time avoiding salt and water retention. The clinical and surgical study was carried out on patients who presented the poorest risks, namely, those whose prognosis was grave, being limited to months rather than to years. Most of these patients had irreversible changes involving heart, brain and kidney. In all, a total of 15 bilateral adrenalectomies were performed. Four patients died of cardiac disease, and three from renal failure. Another patient died of an Addisonian crisis, the nature of which was not recognized while he was visiting a distant city. Another had only recently been operated on. The remaining six are alive, five being very well. The presence of renal failure is now considered to be a contraindication to bilateral adrenalectomy.

Discussing pre-operative preparation and operation technique, Harrison, Thorn and Criscitiello explain that it is preferable, and has even been proved safer, to perform the bilateral operation in one stage. During the period of pre-operative study, efforts are directed towards obtaining maximal circulatory efficiency, and restoration of cardiac and renal function. A salt-free diet, diminution of oedema by diuresis, digitalization and sedation are fundamental. Cortisone, 100 milligrammes, is given intramuscularly the night before operation. Continuous spinal analgesia is considered to be safer for these hypertensive patients, but intratracheal ether anaesthesia makes a better exposure possible. During operation, aqueous

adrenal cortical extract (100 to 200 millilitres) and "Neosynephrine" (20 to 50 milligrammes) are given by intravenous drip as required for circulatory stability. Cortisone, 50 milligrammes every six hours, is given intramuscularly during the first forty-eight hours after operation, and this is gradually reduced to 35 to 25 milligrammes per day as a maintenance dose. A sodium chloride diuresis usually occurs in the first ten days after operation; so in the late post-operative care salt depletion with resultant weakness and hypertension must be avoided by the addition of three grammes or more of sodium chloride per day, and DOCA, one milligramme per day, three to six times a week as necessary. Some patients do not need the DOCA.

The first recorded account of bilateral total adrenalectomy in man, with survival of the subject, appears to be that of Charles Huggins and W. W. Scott,² who performed the operation in 1945 for reactivated carcinoma of the prostate. In 1950 D. M. Green *et alii*³ reported bilateral subtotal adrenalectomy for malignant hypertension and diabetes; review after nine and fifteen months revealed arrest in progress of the renal lesions, with regression of cerebral, retinal, myocardial and vascular disturbances, and greater control of the diabetic state. C. C. Wolferth *et alii*⁴ report initially promising results in cases of otherwise intractable hypertension from subtotal (95%) bilateral adrenalectomy combined with bilateral splenectomy and bilateral sympathectomy. In their series Harrison, Thorn and Criscitiello have used the posterior approach described by Hugh Young, chiefly because it confers bilaterality to the operation, and because the patient's position is well adapted to continuous spinal anaesthesia. The prone patient is flexed at the trunk, with the thighs lowered to a 20° angle, and abdominal compression is avoided. The incision is made over the twelfth or even the eleventh rib. The rib is resected subperiosteally, the subcostal muscles in the rib bed are incised, the lumbo-dorsal fascia is divided and the peri-renal fascia is opened. Care is taken to avoid opening the pleura in the costo-vertebral angle. The kidney is partially mobilized and displaced caudally. The largest vessels enter and leave the adrenal gland superiorly, joining the phrenic vessels, and inferiorly, to join the renal vessels, the aorta and the *vena cava*. By dividing the superior and lateral attachments first, a better exposure of the medial aspect of the gland is obtained. At this point, a rubber-covered pulmonary clamp is applied to the gland, and gentle traction is made to expose the inferior and medial vessels. On the left side, the splenic vessels cross the operative field, and should be carefully avoided. The right adrenal may be embedded in the inferior surface of the liver, or be in intimate contact with the *vena cava*.

In summing up their work, Harrison, Thorn and Criscitiello state that this study was not undertaken with the idea that the adrenal was the cause of malignant hypertension, but rather that it was one important factor because of its production of desoxycorticosterone-like substances, and that the effects of eliminating the salt-retaining influence deserved investigation. It was fully recognized that most of the patients would not be able to tolerate a drastic fall in blood pressure, but that circulatory efficiency might be improved by effective alteration of salt and water metabolism, and that possibly an arrest of the progressive vascular disease might be attained. The former result has been achieved; judgement on the latter will depend on studies of the subsequent course of these patients. In the discussion which followed the presentation of Harrison, Thorn and Criscitiello's paper by Harrison at the annual meeting of the American Urological Association, Dr. Charles Huggins, a pioneer of the operation of adrenalectomy, said that they had just listened to one of the great papers of the age. He confessed that he was a little more enthusiastic than Harrison. Most observers will probably prefer to share Harrison's conservatism, while watching further developments with interest.

¹ *Annals of Surgery*, December, 1945.

² *The Journal of the American Medical Association*, October, 1950.

³ *Annals of Internal Medicine*, July, 1951.

Abstracts from Medical Literature.

MEDICINE.

Sulphaguanidine.

L. H. LONERGAN (*The American Journal of the Medical Sciences*, January, 1952) discusses the absorption and excretion of sulphaguanidine. He states that the general opinion was that sulphaguanidine was poorly absorbed from the digestive tract. However, it has been shown that with patients on maintenance doses a blood level of two milligrams per 100 millilitres is usually reached. Twelve normal subjects were observed in this study after taking 0.25 to 0.38 grammes of sulphaguanidine every four hours. Blood levels of 0.70 to 1.29 milligrams per 100 millilitres were recorded. Urinary excretion was found to be 47% to 107% of the twenty-four hours' intake. The conclusion is that sulphaguanidine is readily absorbed from the digestive tract when given in small doses.

Aureomycin Given Per Rectum.

A. C. SIEGEL, G. H. NICKERSON AND C. D. COOK (*The New England Journal of Medicine*, March, 1952) present evidence to show that aureomycin cannot be given effectively *per rectum* in children. Even with large doses absorption was very variable and serum concentrations were inadequate. Side effects included mucosal irritation, tenesmus and pain.

Quinidine.

M. J. BINDER AND L. ROSSO (*The American Journal of Medicine*, April, 1952) report two cases of paroxysmal ventricular tachycardia and fibrillation due to quinidine. They state that paroxysmal ventricular tachycardia has been reported in a number of cases following administration of quinidine, even in small doses. Two doses of 0.2 grammes of quinidine sulphate given orally have given rise to ventricular fibrillation in two reported cases. The authors report two similar cases occurring during an attempt to convert auricular flutter and fibrillation to normal rhythm. In the first case, 0.8 to 1.2 grammes of quinidine given daily did not prevent attacks of auricular flutter. The patient was then treated with 0.4 gramme given thrice daily for one week, then 0.2 gramme every two hours for six doses, and then 0.2 gramme eight times daily for two days. Ventricular tachycardia began; digitalis did no good; eventually the heart rhythm became normal. The other patient had auricular fibrillation, then developed ventricular tachycardia, had Stokes-Adams attacks, but eventually recovered from the treatment.

Procaine Amide.

N. S. STEARNS *et alii* (*The Journal of the American Medical Association*, February 2, 1952) discuss the value of intravenous procaine amide ("Promestyl") therapy in the treatment of ventricular arrhythmias. Thirty-three patients were treated; ventricular tachycardia was converted to a slower supraventricular rhythm in six cases.

However, other irregularities, such as auricular fibrillation, occurred in some. In two cases the condition was unchanged. In some cases severe hypotension occurred with the doses given, 200 to 800 milligrams. In one resistant case, the ventricular tachycardia was converted with quinidine, and the patient quickly died. Ectopic ventricular beats were eliminated in eight out of twelve cases. Nodal tachycardia responded in two cases. Auricular fibrillation did not respond. In thirteen cases a dangerous fall of blood pressure occurred. In two out of four cases of bronchial asthma, intravenous procaine amide therapy produced convulsions, and it did not stop the asthmatic attack in the other two. The value of the drug appeared to the authors to be doubtful.

Pitressin in Rheumatoid Arthritis.

G. G. HAYDN AND B. W. HAYDN (*The American Journal of the Medical Sciences*, January, 1952) describe the short term effect of pitressin in rheumatoid arthritis. Four units of pitressin were given intramuscularly. Pain and stiffness diminished in the affected joints. Traumatic or osteoarthritis joint lesions were not affected. The authors state that ACTH induces a remission in rheumatoid arthritis through the adrenal cortex. Pitressin may act in the same way, though the effect of pitressin occurs within thirty minutes. At the same time a considerable increase in the number of eosinophilic cells occurs in the blood. The relief of pain and the eosinophilia last for about twenty-four hours. The authors consider that the heightened adenosintriphosphatase activity of tissues underlies the rheumatoid process.

Lupus Erythematosus.

S. A. M. JOHNSON AND O. O. MEYER (*The American Journal of the Medical Sciences*, January, 1952) discuss the treatment of *lupus erythematosus disseminatus* with cortisone. Nine patients were treated. Varying doses were used, including continuous doses of 100 to 200 milligrams daily up to a total of six grammes. Other patients were given 200 milligrams daily for ten days with repetition of therapy after twenty-day intervals for two subsequent courses, up to six grammes in all. All patients improved to a degree, but relapse followed cessation of treatment. The authors state that cortisone is probably most useful to tide patients over acute episodes.

A New Ulcer Drug.

M. P. ROGERS AND C. L. GRAY (*The American Journal of Digestive Diseases*, June, 1952) describe the effects of treatment with a new anti-ulcer drug. They state that "Trasentine" hydrochloride and its homologues produce functional inhibition of the intestinal tract. A new one, Ba-5473 (phenylcyclohexyl-oxyacetic acid-diethylaminoethyl esterbrommethylate) (Ciba) has sympathetic ganglionic blocking ability and gastric antisecretory and antacid properties. It was more effective in preventing peptic ulcers in the Shay rat than either atropine or "Banthine". This drug was tried out on rats and laboratory volunteers before being used for peptic ulcer patients. At first a dose of 25 milligrams every six hours was given, but soon this was changed

to 10 milligrams three times daily and at bedtime. On this regime all ulcers were healed in twenty-four patients within three weeks to three months. Side effects depending on the dose were dry mouth, epigastric fullness due to gastric dilatation, and mild constipation. The authors advise further tests of the drug.

Banthine.

C. G. MCARDY *et alii* (*The Journal of the American Medical Association*, December 22, 1951) report on "Banthine" (methantheline) bromide in gastro-enterology. They state that this anticholinergic inhibits acetylcholine production, and it reduces salivation and gastric secretion. Gastric and colonic motility is diminished, but patients with colon disorders do not benefit. With irritable and spastic colon there is little benefit. Cardiopasm is not relieved. Painful acute pancreatitis is relieved.

ACTH and Cortisone in Nervous Diseases.

G. H. GLASER AND H. H. MERRITT (*The Journal of the American Medical Association*, March 15, 1952) describe the use of ACTH and cortisone in nervous diseases. They state that 80 to 100 milligrams were given intramuscularly for five days to two weeks. In cases of multiple sclerosis, transient benefit for spasticity and bladder disorders was noted. Patients with amyotrophic lateral sclerosis did not benefit. Those with progressive muscular dystrophy and *myotonia atrophica* did not improve. Those with Wilson's disease and Sydenham's chorea did not respond to ACTH or cortisone.

Rheumatoid Arthritis and Gout.

W. C. KUZELL, R. W. SCHAFARZICK AND B. BROWN (*The Journal of the American Medical Association*, June 21, 1952) describe the use of phenylbutazone ("Butazolidin") and a mixture of aminopyrine and phenylbutazone, known as "Irgapyrin" in Europe and "Butapyrin" in the United States of America. The authors state that aminopyrine is well known for its toxic effect, hence the trial of phenylbutazone alone. This drug was given orally in tablets of 125 or 200 milligrams, one to six times daily. In gout, phenylbutazone was of more value than colchicine in some patients, who responded in forty-eight hours. Intramuscular injection of a 20% solution of the sodium salt of phenylbutazone was effective also. In general, the authors favoured the use of phenylbutazone in gout. In rheumatoid arthritis and osteoarthritis the authors also claim that valuable results were obtained so long as the drug was given. In some patients, phenylbutazone gave better results than cortisone; in others the drug gave good response when given at the same time as cortisone; other patients obtained most benefit from cortisone alone. For osteoarthritis, osteoporosis of the spine, rheumatoid arthritis with psoriasis, and acute peritendinitis of the shoulder, improvement was recorded. In the last-named complaint prompt and complete relief of symptoms was noted in five out of eight patients. Toxic reactions caused a cessation of treatment in 17 out of 140 patients treated. Forty-

seven patients in all had toxic reactions. Measly rash, oedema, nausea, activation of peptic ulcer, vertigo and anaemia were observed. There was no leucopenia. Experiments in rats showed that while corticotropin (ACTH) diminished adrenal ascorbic acid content, phenylbutazone and other pyrazolidines did not. Oedema due to phenylbutazone was reduced by a low sodium diet. The development of peptic ulcer should be prevented by the use of antacids.

Amoebicidal Drugs.

W. A. SODEMAN AND P. C. BEAVER (*The American Journal of Medicine*, April, 1952) report a study of the therapeutic effects of some amoebicidal drugs. Amoebiasis among patients in a mental hospital in Mississippi was studied. *Entamoeba histolytica* was found in the stools of 22% of the patients. The following drugs were studied: "Diodoquin", three tablets of 0.21 gramme per tablet, given thrice daily for twenty days; chiniofon, four pills of 0.25 gramme each, given thrice daily for eight days; "Milibis", two tablets of 0.25 gramme each, given thrice daily for eight days; and thioarsenites, two tablets of 0.05 gramme per tablet, given thrice daily for ten days. "Diodoquin", "Milibis" and thioarsenites gave good results in eliminating *E. histolytica*. Chiniofon was less effective. Thioarsenites were most effective, as they eliminated *E. coli* and *E. nana* as well as *E. histolytica*. "Milibis" and "Diodoquin" were the next best drugs. Toxic reactions from the drugs were rare. "Milibis" is an arsenical bismuth compound introduced in 1948 by Hauer.

Neomycin.

V. S. LIVINGGOOD *et alii* (*The Journal of the American Medical Association*, February 2, 1952) describe the results of treatment of pyogenic infections with neomycin. They state that this antibiotic is produced by *Streptomyces fradiae*. Freely soluble in water and heat-stable, it does not lose its potency in any type of vehicle. *In vitro*, neomycin is effective against a wide variety of organisms. In the human subject, however, injection of neomycin has toxic effects on kidneys and on hearing, in doses of two grammes daily. Given orally one gramme of neomycin every four hours promoted intestinal antisepsis in abdominal surgery and was not absorbed to any extent. The authors used neomycin as a topical application in skin diseases due to or complicated by the presence of pyogenic organisms. Impetigo, paronychia, boils and styes, pustular folliculitis, *otitis externa* and secondarily infected burns all responded rapidly to an ointment containing five milligrammes of neomycin sulphate per grain in a base of paraffin and lanoline. A watery solution of neomycin sulphate, one milligramme per millilitre, was equally effective as a compress or soak. No toxic effects were observed in 264 patients treated by these methods.

R. L. KILE *et alii* (*ibidem*) praise the use of neomycin in dermatology. In 675 patients the results of treatment of primary and secondary infection were studied mainly. Ointments (five milligrammes per grain) and watery solutions (one milligramme per millilitre) were used. The best results were obtained in infectious eczematoid

dermatitis, folliculitis, impetigo and secondary pyogenic infection. The ointments caused irritation in several patients. Only one proved case of sensitivity occurred. All staphylococci were sensitive to neomycin *in vitro*. Some patients with haemolytic streptococcal and pyocyanous infections did not respond well to neomycin.

Amoebiasis.

L. V. MCVAY, R. L. LAIRD AND T. N. STERN (*The American Journal of the Medical Sciences*, January, 1952) describe the treatment of amoebiasis with neomycin. They state that other antibiotics have been used with poor results. "Chloromycetin", bacitracin and penicillin have been praised by some and condemned by others. Aureomycin has been favourably reported on by several observers. Six patients were given 50,000 units of neomycin by mouth every three hours for one day, then 50,000 units every six hours until 1,600,000 units had been given. Three of these patients became free of amoebae for three months, the others relapsed within fourteen days. These last-mentioned patients had six to twelve "negative" stools after treatment. They were given three times the amount of neomycin at this stage, and have been free of amoebae for three months since treatment. One toxic effect noted was the effect on the kidneys of one patient; albuminuria and raised blood urea content were noted, but these returned to normal when administration of neomycin was ceased. Slight nausea and diarrhea were noted in three other cases. Investigators are warned of the toxic effects of neomycin.

Parenteral Administration of "Ammivin" (Khellin) in the Treatment of Angina Pectoris.

ESTELLE E. KLEIBER (*Annals of Internal Medicine*, May, 1952) states that oral administration of the antispasmodic drug khellin has had many trials in the treatment of angina pectoris. Unpleasant side effects, especially gastro-intestinal ones, have, however, been unduly frequent. Because of this, intramuscular administration of khellin ("Ammivin") was tried in the treatment of 18 ambulatory patients with *angina pectoris*. All had been under treatment with a variety of drugs before this trial. Patients were advised to continue using nitroglycerin when needed, but other drugs were omitted when possible. The dosage in most cases was 50 milligrammes of khellin (one millilitre of "Ammivin") as an initial dose, and then 100 milligrammes once per week over a period of many months. Gastro-intestinal disturbances with this dosage were entirely absent. When the frequency was increased to every two or three days, nausea and vomiting often appeared. Results of this treatment were encouraging, and most patients noticed less frequent and severe attacks and a reduced need for auxiliary medication.

Needle Biopsy of the Liver.

JOHN M. RUMBALL (*The American Journal of Surgery*, August, 1952) states that at his hospital 308 needle biopsies of the liver have been performed on 280 patients in nearly five years. This procedure is now a definite part of his diagnostic armamentarium

in the differential diagnosis of primary liver disease and is an aid in lending light to some undisclosed conditions. He describes his technique with a Vim-Silverman needle and states that he prefers the intercostal or transpleural method. The patients are given 10 milligrammes of vitamin K three times a day by mouth prior to the biopsy regardless of the prothrombin time. In general, needle biopsy is of benefit in diagnosis of any case of primary liver disease, which may include the following: (i) parenchymal and extrahepatic biliary obstruction which have to be differentiated, (ii) cirrhosis of the liver, (iii) hepatitis, (iv) hepatomegaly of undetermined cause. Needle biopsy is also indicated with some of the following systemic diseases or diseases in which the liver is involved secondarily: (i) pulmonary and abdominal malignant disease, (ii) systemic disease, (iii) systemic diseases unrecognized, such as tuberculosis, sarcoidosis and brucellosis. The following contraindications, although few, must be strictly observed: (i) disturbance of coagulation of blood, including an abnormal prothrombin time; (ii) the presence of abdominal ascites, which makes needle biopsy of the liver very difficult and often impossible; (iii) pulmonary disease involving the lower part of the right lung or right pleural cavity; (iv) inability of a patient to cooperate by holding his breath at the proper time.

Papilloedema and the Guillain-Barré Syndrome.

ARTHUR L. DREW AND KENNETH R. MAGEE (*A.M.A. Archives of Neurology and Psychiatry*, December, 1951) report on the incidence of papilloedema in the Guillain-Barré syndrome. They state that a review of all available literature resulted in the finding of only nine documented cases of papilloedema in this syndrome. They report a tenth case, and conclude that at present, on the general hypothesis of the mechanism of papilloedema, there is no satisfactory explanation of the occurrence of papilloedema in the Guillain-Barré syndrome. They request careful observation and reporting of all cases in which it is observed.

Papilloedema in Poliomyelitis.

CLINTON G. WEIMAN, FLETCHER H. McDOWELL AND FRED PLUM (*A.M.A. Archives of Neurology and Psychiatry*, December, 1951) report on five cases of poliomyelitis in which papilloedema was found during the convalescent period. The five patients were taken from the series of 106 patients admitted during 1949 and 1950 to the New York Hospital. The findings were remarkable owing to the rarity of optic fundal changes in poliomyelitis. The patient's ages ranged between eighteen and twenty-eight years. They had severe paralysis, and the papilloedema appeared from eleven to forty-eight days after the onset of the illness and lasted thirteen to one hundred and forty days. Each patient complained of diplopia, and one had a headache in addition. The visual activity and fields were normal in the five cases, and three patients examined by lumbar puncture had a raised cerebro-spinal pressure. The papilloedema was a benign complication of the disease, and the authors consider it to be part of a generalized edema of the central nervous system associated with the acute infection.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

XLI.

ETHICS IN MEDICAL CONSULTATION.

In the medical life the practice of consultation is intended only to be of benefit to the patient and advantage to the doctor. Yet its effect may produce disharmony, either between doctors or between their patients and themselves.

This explains why the ethical rules governing consultations are numerous and detailed, and need to be fully understood by every medical practitioner. Essentially they are the means of enabling a patient, while under the care of one doctor, to receive the services of another, without infringement of the ethical code as it deals with super-session. The rule to be observed particularly is that it is unethical for one practitioner to attend a patient who is under the care of another, without having satisfied himself that the latter has been informed that his services are no longer required.

It is obvious to a doctor that without such a provision there would be a very real danger of a patient having two or more courses of treatment together. But undoubtedly patients often consider it an objectionable restriction of their freedom of choice that they may not obtain another opinion at any time they desire it. Practitioners should therefore not be surprised, or unduly annoyed, when a patient says frankly that he will not conform to the rule. Many a misunderstanding would be avoided if some doctors would take a more tolerant attitude on such occasions, allowing for the wide variation of standards and views among those concerned.

In illustration of this the rule may be quoted: "It is the duty of an attending practitioner to accept the opportunity of consultation in obscure and difficult cases, or when consultation is desired by the patient, or by persons authorized to act on the patient's behalf." This implies that when the approach is made by the patient it should be received in a courteous and friendly way. It should be appreciated that the patient is in a somewhat invidious position in that, by the very circumstance of his making the approach, he reveals that he is not quite satisfied with the position. And it must be emphasized that, as Saunby says, "patients are not anybody's property". No practitioner loses in dignity by agreeing to a consultation. Yet there is good reason to believe that on some occasions a request for a consultation is regarded as an outrage to professional dignity; the approach is coldly received, sometimes even rebuffed, though this is a breach of ethics.

It is not surprising then that the patient who desires another opinion, but feels that the suggestion would be resented, may go behind the doctor's back in obtaining it. Often, however, there is a genuine desire to avoid hurting the feelings of a trusted family doctor. And some, unable to credit anything but collusion in a consultation between two doctors, are actuated by determination to obtain what they call an independent opinion.

The safeguard against these and other possible discords is a good-humoured understanding of human nature.

Among other rules of consultation is one, made long ago in England, which needs to be interpreted with allowance for the modern standard of public education in health matters. It says: "The attending practitioner should nominate the practitioner to be consulted and advise accordingly, but he ought not to refuse to meet a practitioner selected by the patient, or the patient's representative, although he is entitled, if such is his opinion, to urge that the practitioner selected has not the qualifications or the experience which the particular demands of the case require." When this was phrased people were much less health-conscious, and less familiar with the names of those in consulting practice, than is the Australian public today.

The doctor should therefore, if invited to nominate a consultant, preferably mention the names of two or three suitable persons; he will make the final selection only if requested to do so. Otherwise the patient, directly one name is given, may ask if someone else is not as good, or better. And in practice, when it is the patient who seeks the consultation, he usually has his own nomination ready. Unless obviously unsuitable this should not be refused, for the reason that if an alternative choice is suggested, the

impression is likely that the patient is being diverted to one of his doctor's particular friends; a sinister motive may even be suspected. Also it is embarrassing when, as sometimes happens, the determined patient visits the doctor of his choice and tells how a colleague tried to prevent it.

A consultation being decided on, the most satisfactory arrangement is that the two doctors see the patient together. For this enables the regular attendant to inform the consultant, before the physical examination is made, of the events in the illness; and it affords opportunity afterwards for full discussion.

The consultant should then, in the presence of the other doctor, inform the patient and relatives of the joint opinion. As the consultant is present in the patient's interest, his duty, if there should be a real difference of opinion, is to say so, and, if he regards it as essential, to recommend a change in the treatment. At the same time he should avoid any comment that might undermine the confidence of the family in their doctor. Therefore he should particularly avoid suggesting any unimportant or trivial changes in the treatment. Naturally it is when the consultant is able, quite honestly, to confirm the diagnosis, and fully approve the treatment already given, that the consultation is most satisfying for all concerned.

The consultant, afterwards, should resolutely refuse, unless expressly requested by the attending practitioner, to discuss the case in any way—by interview, by letter or by telephone—with any member of the family; for, owing to lay ignorance of medical phraseology, such comments would be very likely to result in misunderstandings.

As to ambulatory patients, it often is most convenient for all parties that the consultant should see them in his rooms alone. The family doctor, then, should supply by letter the fullest possible details of the illness. In his reply, the consultant should fully discuss his findings and any treatment he might suggest. If his views coincide with those of his colleague, it is desirable that he should, at once, so inform the patient. But if he should differ materially, it is as well that he should be as non-committal as possible, while strictly avoiding prevarication; it can be left to the family doctor to explain the position more fully.

In his own consulting room, the consultant or specialist has often to deal with delicate ethical problems. Ideally, he might refuse to see anyone who had not been directed to him by a doctor. But in Australia it has long been the practice to see anyone who seeks advice, and who is not under the care of any other doctor. For it would be difficult to insist that an individual, who was not under medical care, should first visit some doctor he did not wish to see, simply in order to receive a letter to the specialist.

Obvious risks to be avoided here are accepting a patient who is already under medical care, and accepting a patient who not only is already under medical care, but wishes to obtain other advice without the knowledge of the regular attendant. It is some safeguard to instruct the secretary to inquire, when booking appointments, whether the prospective patient is under other medical care, and if so, to state that the patient must be directed by his own doctor.

If it is learned, in the course of an examination, that a patient who has prevaricated is really under other medical care, every endeavour should be made to convert the occasion into a consultation, by getting the patient to agree to a letter being sent to the family doctor. In the few cases in which this procedure is unacceptable, or in which it transpires that a consultation has been requested, and refused, the only course is to inform the patient that he cannot be seen again without the express approval of the regular medical attendant.

Apart from the subject of specialist consultation, ethical problems are often involved in decisions on emergency treatment. Circumstances in which especially it is desirable that the attending practitioner, while dealing with an emergency, should endeavour to secure consultation with a colleague, are discussed as follows:

- When he must consider the propriety of performing an operation, or of adopting some course of treatment, which may involve considerable risk to the life of the patient, or may permanently prejudice his activities or capacities; particularly when the condition to be treated is not dangerous to life.

- When operative procedures involving the death of the fetus or of an unborn child are contemplated, especially if labour has not commenced.

- When continued administration of any drug scheduled under the *Dangerous Drugs Act* is deemed desirable, though only for relief of symptoms of addiction.

4. When there is reason to suspect that the patient has been subjected to an illegal operation, or is the victim of criminal poisoning.

Among ethical rules governing consultations conducted at the patient's residence the following should be observed, unless in any instance there is substantial reason for departing from them.

The attending practitioner should ascertain the consultant's fee, and should inform the patient or his representatives that it should be paid at the time of the consultation.

If the attending practitioner does not keep the appointment, the practitioner consulted may after a reasonable time examine the patient; he should then communicate his findings in writing, and in a sealed envelope, to the other practitioner.

On entering the patient's room, the attending doctor should precede the consultant, who, however, should leave first.

All discussion by the two should be conducted in private.

The opinion, and the treatment as agreed, should be communicated to the patient or his representatives by the consultant, in the presence of his colleague.

Should the two hold divergent views, either on diagnosis or on treatment, and should the attending doctor be unwilling to follow the treatment advised by the consultant, this difference of opinion should be communicated to the patient or his representatives by the consultant and attending doctor jointly. The patient or his representatives should then be advised either to choose one of the suggested alternatives or to obtain further advice.

A consultant should not attempt to secure for himself the care of a patient seen in consultation.

It is the duty of the attending doctor loyally to carry out the measures agreed at, or subsequent to, the consultation.

The consultant shall not supersede the attending doctor during the illness, nor shall he act as attending doctor to the patient in any subsequent illness, except after an explanation given to his former colleague, unless this is in the circumstances impossible. But the rule cannot be followed absolutely where, as in country and suburban practice, consultations are often held with, and assistance given by, general practitioners. However, the more closely the principle is followed the better.

The principle to be observed is that the consultant, whether specialist or general practitioner, must not take an unfair advantage of the doctor who calls him in consultation. And so, for a reasonable time at least, he should refrain from attending any of the near relatives of the patient.

J. G. HUNTER,
Sydney.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on September 25, 1952, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney. Dr. R. H. MACDONALD, the President, in the chair.

The Aetiology and Treatment of Hypertension.

DR. IAN SIMPSON read a paper entitled "The Aetiology and Treatment of Hypertension" (see page 96).

DR. JAMES ISBISTER read a paper entitled "The Aetiology and Treatment of Hypertension" (see page 99).

DR. GASTON BAUER referred to the use of hexamethonium bromide in the treatment of hypertension, and said that it was at the moment the most promising, if not the only, medical weapon. He had learnt to use it at the Post-Graduate Medical School of London under Professor McMichael. It was a powerful pharmacological agent and had many side effects. It could not be given as a substitute for phenobarbitone, and it had to be given with due respect for its potency. It should be reserved for the severest forms of hypertension—cases in which progressive severe fundal changes and true hypertensive symptoms not relieved by ordinary measures were observed, and cases in which the diastolic blood pressure in young people was rising over

130 millimetres of mercury. To hexamethonium bromide could be applied the words used at Paris in September, 1950, by Kempner referring to the rice diet—it could be dangerous or ineffective. It had been found to be both. Dr. Bauer cited the example of the patient in whom a dramatic fall in the blood pressure occurred after an intravenous dose of something like five milligrammes, which was 1000 times less than the oral dose sometimes employed. There was at the present moment no short cut to hexamethonium therapy. If a patient was severely enough affected for this drug to be indicated, the parenteral route should be used first, and later a change could be attempted to the oral route. Dr. Bauer, in conclusion, repeated that hexamethonium bromide was the most promising drug at present, but better and less toxic drugs could be expected in the future.

DR. W. J. McCRISTAL, in the course of his remarks, said that he failed to see why the use of hexamethonium bromide in hypertension was favoured. He thought that the word "treatment" might with advantage be expunged from present thought on hypertension. The word "management" was a much more suitable term. After hearing Dr. Simpson's remarks on the emotional side, including the problems and needs of the patient, Dr. McCristal thought that those present must have felt that their fate in that direction was inescapable. It was not wise to ignore the electrocardiogram. If used properly, it might help to explain why many hypertensives had for so long escaped a cardio-vascular syndrome.

DR. JOHN GRANT said that, as a surgeon, he was interested in hypertension mainly from the point of view of sympathectomy. He had two questions to ask. The first was based on the well-known fact that in many cases of hypertension treated by sympathectomy, although the blood pressure did not fall, the symptoms were relieved. The question he wished to ask was whether the same thing happened as a result of treatment with the recently introduced drugs. Dr. Grant's second question was whether any of those present had had experience of using the drugs in cases in which sympathectomy had been performed and had failed.

DR. J. D. RUSSELL said that as a psychiatrist he felt that his specialty had almost arrived socially, since one of their number had been promoted to taking part in the meeting and reading a paper. Dr. Simpson's paper had been broad and judicial. The temptation from the psychiatric angle was perhaps to claim a little too much; Dr. Simpson had not done so. He suggested that the psychogenic factor in the aetiology of hypertension might or might not be important. The onus was very much on the doctor to evaluate the personality structure of the patient and to see whether it mattered or not. A view he had cherished for many years, regarding it as a certain thing in an uncertain world, was that hypertension was a disorder thrown up by the materialistic and competitive society in which humanity lived. Dr. Simpson's paper cut across that view and suggested that surveys made in uncivilized communities showed that the rate of hypertension was high. One survey had been made in the Virgin Islands. If the inhabitants were anything like the name of their islands, various frustrations might account for that state of affairs. Dr. Russell was interested in the conditions under which the patient's blood pressure was measured, and he asked Dr. Isbister whether any attempt could be made to standardize them. He pointed out that a woman patient might arrive for examination after a rush to get to the surgery in time, or an aggressive type of man might arrive and be kept waiting, and in each case the blood pressure would very likely be raised. All patients admitted to the Repatriation General Hospital, Concord, underwent a physical examination and had their blood pressure measured on their arrival, and the blood pressure figures were often high. Ambulatory psychiatric patients had their blood pressure measured again a week or two later, and the figures were frequently totally different. Dr. Russell wondered whether it would be possible to standardize some of the environmental conditions. He felt that hypertension was a disease in which they as doctors frequently bore some degree of responsibility for increasing rather than relieving the anxiety of the type of patients affected. He was not sure that doctors appreciated the amount of fear and anxiety that accompanied the approach of many of their patients to them. He himself had spent half an hour or so in a colleague's surgery waiting to be examined, and had been surprised at the degree of his own tension. All patients with hypertension badly needed reassurance, and they needed to be able to talk to the doctor. In a disease which would last for many years and about which so little was known, their approach to the patient must be to give him confidence, support, and where possible understanding.

DR. W. A. SELDON said that he had a question to ask Dr. Isbister. It had been said during the meeting that the hexamethonium compounds were the most potent drugs in use; they had always seemed to him to be unphysiological. Kempner's rice diet was physiological, but unpalatable. With the cation exchange resins it was possible to give the patient a palatable diet and keep down absorption. Dr. Seldon wondered whether Dr. Isbister could give any views on that possibility.

DR. W. E. FISHER said that he agreed with Dr. Isbister that they should seek with more care than usual for the secondary type of hypertension, because in the majority of cases the treatment was that of the condition to which the hypertension was secondary. Therefore he did not altogether agree with Dr. Isbister's suggestion that one should not be over-enthusiastic in the investigation of a patient when hypertension was first recognized. He thought the opposite, especially in relation to excretion pyelography. In any large series of cases, renal lesions of surgical type would be found to be present in no less than 10%. Some of the lesions would be amenable to surgical treatment, others would not; but patients should not be denied the chance of having something done at that early stage when the cause would not be revealed by, for example, investigation of the specific gravity of the urine. The more important part of the hypertensive population was the essential group. If one observed patients whose records were available over a period of twenty years, one could find such instances as a first blood pressure reading up to 200 millimetres of mercury, systolic, and twenty years later a reading of apparently the same level, no progress having been made. One could infer that the level had remained steady throughout the period. Again, one could find a case in which the systolic blood pressure was back to a reasonably low normal level of 140 millimetres of mercury. One could find a patient who had had a negligible rise in blood pressure. One could find a patient whose systolic blood pressure was 160 millimetres of mercury when first recorded, who remained symptom-free, and by chance eight or nine years later a figure of 300 millimetres of mercury might be found a fortnight before the patient died. Dr. Fisher said that his point was that the dangerously rapid rise was always a possibility. As Geoffrey Evans had said, symptoms were a reflection of activity of the hypertensive process, associated with rapid changes in the blood pressure, rather than its absolute level, unless at excessively high levels. All forms of treatment, old and new, could be of some assistance; but if any drastic result was to be achieved, then it should be possible to begin treatment early and do something before it was too late. Dr. Fisher said that he thought patients should be told that an elevation of blood pressure had been found. He agreed that an iatrogenic reaction was possible, but not necessarily; in telling the patient what he had found the doctor need not do damage—he should rather enlist the patient's cooperation. He said that no one could deny the value of education in *diabetes mellitus*; and the same procedure should be followed in hypertension, as had already been done by Irvine Page. He concluded that they could do good in hypertension.

Dr. Simpson, in reply, referred first to Dr. Isbister's paper, in which had been mentioned Robert Platt's theory of the hereditary factor. Dr. Simpson said that it was convincing; but if they talked in terms of heredity and put it as one of the aetiological factors, a slight cloud was put over therapy, the deduction being that hypertension was all due to genes. Platt was an organic-minded person, and possibly had not made much assessment of environmental factors. As he (Dr. Simpson) had said, the way of life might be inherited rather than the hypertension itself. Hypertension was commonly seen in fairly obese people, and it was known that over-eating was one means of obtaining emotional satisfaction. Some hypertensive people, who were said to be inhibited in emotional outlets, might find a certain amount of satisfaction in over-eating. How many really gave up their attitude towards food and followed their diets strictly? He himself had not had much success with his patients. With regard to phenobarbital, Dr. Simpson said that perhaps it was useful; but when a neurogenic factor was operating, he thought it better to do something about that. If that was not done, the prescribing of phenobarbital was like treating pneumonia with a cough mixture. The thing to do was to deal with the patient's mode of life, and help him to deal with his worries in a better way. Dr. Simpson said that he made no claim that certain personality factors were characteristic, but they were commonly found; the patients had the type of personality in which there was a conflict between aggression and submissiveness. To Dr. Grant, who had mentioned the relief of symptoms by sympathectomy,

Dr. Simpson said that symptom relief could be achieved by the administration of 10 minims of dilute hydrochloric acid three times a day. Any treatment given with conviction could achieve good results symptomatically. There were pronounced differences in the response to the cold pressor test when the patient knew that the outcome would decide whether or not operation was to be performed. In reply to Dr. Fisher, Dr. Simpson said that how patients were told about the findings was important, but even more important was which patients were told. Some could not tolerate any knowledge at all. The method of enlightenment had to vary with the individual. A good rule was to teach the truth in small doses.

Dr. Isbister, in reply to Dr. Grant and Dr. Simpson, said that he took it that when they spoke of the relief afforded by sympathectomy, they were referring to such things as severe headaches, impairment of vision, shortness of breath and so on. He thought that they were relieved even if the blood pressure was not much lower. The same applied to hexamethonium bromide. He himself had had no experience with the use of that drug when sympathectomy had failed, but he believed that it had been used with some benefit. Dr. Isbister agreed that the conditions under which the blood pressure was measured were not standardized. However, most physicians measured the blood pressure after the period of history-taking; it was not very long, but perhaps it was long enough for the patient to recover from the initial apprehension. If the measurement of the blood pressure was left until the end, that made the conditions as standardized as possible. Conditions in his own cases were fairly standardized—the patients were examined in hospital wards, or single rooms, in the out-patient department. It was impossible to do much better. Dr. Isbister went on to say that cation exchange resins had been used in the treatment of hypertension, but he had had no experience of them. If the methonium salts were in the experimental stages, the cation resins were even worse. The dangers of their use were far too great; they should be used only where there was adequate control of electrolytes. Dr. Isbister said that he had not meant to give the impression that patients with hypertension should not be investigated at all; what he had meant was that intravenous pyelography was a most important investigation. It was the only way to diagnose renal disease in the treatment of which surgery might be useful. However, good history-taking would give most of the answers and most of the clues to what would be desirable.

Dr. Macdonald, from the chair, thanked Dr. Simpson and Dr. Isbister for their papers, and those who had taken part in the discussion.

A MEETING of the New South Wales Branch of the British Medical Association was held on September 18, 1952, at Sydney Hospital. The meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital.

Hirschsprung's Disease.

DR. S. L. SPENCER presented two adolescent patients with Hirschsprung's disease. One of the patients had been treated by procto-sigmoidectomy, while the other had responded to medical measures.

The first boy was aged fifteen years, and had been referred about eighteen months before by Dr. Alan Young. There was a history of bowel difficulties typical of Hirschsprung's disease since birth, and the patient had had a presacral neurectomy performed at the age of seven years, without benefit. Since then his condition had become steadily worse, and when he was first examined he was having great difficulty with his bowels, which had not acted without enemas for nine months. Accumulations of flatus had caused him severe discomfort, and he found it necessary to lie on his abdomen before he could expel it. His disabilities were interfering seriously with his progress at school. Physical examination showed the patient to be pale and undersized; he had a grossly distended abdomen, the site of visible and audible peristalsis. X-ray examination showed huge dilatation of the transverse, descending and upper part of the sigmoid colon with a small deflated segment below that level. At laparotomy the X-ray findings were confirmed, and the junction between the deflated and dilated bowel was marked with three black sutures. The dilated bowel had a diameter of about six inches. A transverse colostomy was also established. Four months later procto-sigmoidectomy was carried out by Denis Browne's method,

and one month later the colostomy was closed. Histological examination of the narrowed lower segment by Dr. L. R. Finlay Jones showed an absence of ganglion cells in the wall of the bowel and plentiful bundles of nerve fibres. For a time after operation bowel washouts every second day were used, not because the patient felt the need of them, but because some faecal accumulation could be felt in the left lower quadrant of the abdomen. They had been suspended for the past six months, and the patient had gained over two stone in weight and was well. The result had been most gratifying, and the patient measured the success of the operation by the fact that he could for the first time swim under water.

Dr. Spencer's second patient with Hirschsprung's disease was a youth, aged seventeen years, who had been referred by Dr. A. C. Herrington. The patient gave a similar history to the previous patient, but less severe, and at the age of two years had had an operation through an abdominal incision whose nature had not been established. The patient remained fairly well until a few months before he was first examined, when, as the result of a domestic upset, he left home and went to live at a guest house. Since leaving home he had had increasing constipation, loss of weight, and abdominal pain and rumblings. Physical examination of the patient revealed a grossly distended and writhing bowel. Opaque enema examination revealed pronounced dilatation of the descending colon and the sigmoid colon. The patient was advised to return to his parents' home and to undergo strict medical treatment, including the taking of paraffin and the use of enemas. He was examined again three months later, by which time his condition had become worse, and he had obstinately refused to return home. On that occasion operation was seriously considered; but it was decided to repeat the earlier advice and to defer a decision for a further period of three months. When he was examined just before the meeting, the youth was found to have made a very satisfactory recovery from the clinical viewpoint, though X-ray examination still showed great dilatation of the bowel. He then explained that he had not returned home, but that he had changed his accommodation. At the first boarding-house the meals had consisted largely of tinned foods, such as baked beans and spaghetti, but his second residential had provided much better and more varied meals.

Dr. Spencer pointed out that the treatment of Hirschprung's disease had undergone a radical change with the introduction in the last few years of the operation of proctosigmoidectomy, in which the apparently normal small lower segment of bowel was removed instead of the grossly dilated and apparently diseased bowel above. Most of the work had been done on infants. In the United States a one-stage resection seemed to be used, while in England a two-stage procedure was preferred. It was interesting to note that recent communications by the State of Minneapolis advised a somewhat different resection. The State recommended that the portion of bowel to be removed should include the dilated part, which he considered did not usually regain normal peristaltic efficiency, together with the collapsed segment only as far as the upper part of the rectum. That operation had the great advantage, in his view, of avoiding the risk of causing impotence from injury to the *nervi erigentes*, which had apparently occurred in some cases after proctosigmoidectomy. Dr. Spencer expressed the view that that new suggestion was of great interest, and that it would appear to have the further advantage of permitting a one-stage resection. He was happy to say that his patient had not become impotent after resection.

Carcinoma of the Penis.

Dr. Spencer's third patient was a man, aged fifty-three years, a motor-truck driver. He had been examined two years previously, when he gave a history of swelling of the penis of six weeks' duration and of urethral discharge. He also complained of a swelling in the right groin. There had been no previous illnesses, but the patient said that it had been impossible to retract his foreskin at any time in his life.

Physical examination showed the patient to be a man in good general condition, but with phimosis and club-shaped swelling of the end of the penis about three inches long and two inches in diameter. Commencing ulceration was present on the left side of the foreskin, and large hard inguinal glands were felt on both sides, those on the right being larger than those on the left.

A partial amputation of the penis was performed, and followed a fortnight later by bilateral dissection of the inguinal glands, of which those on the right side were found to be involved by metastatic deposits. The patient was

examined by Dr. F. Duval, who arranged for both inguinal regions to be treated by deep X rays. The amputation specimen was examined by Dr. E. Hirst, who reported in the following terms: "A growth measuring 7.0 centimetres by 4.0 centimetres is present. The microscopical picture is that of an early developing squamous-celled carcinoma." The glands were examined by Dr. A. A. Palmer, who stated that "metastases are present in the glands from the right groin. Those from the left side show no evidence of malignant deposit". The patient had made very satisfactory progress since operation and was back at work. He found it necessary to sit down to pass urine, but passed a good stream and had no other difficulty. Dr. Spencer pointed out the interest of the association of phimosis with carcinoma.

Aneurysm of the Innominate Artery.

Dr. A. E. McGuinness showed a male patient, aged sixty-two years, who had an aneurysm of the innominate artery. Dr. McGuinness said that the case was notable in that symptomless aortic regurgitation was diagnosed after a routine X-ray examination in 1946 had revealed that the heart was enlarged. The serological findings were positive, and the patient was treated with penicillin by intramuscular injection at intervals of one year, having finally been given a course of 10,000,000 units over a period of fifteen days in November, 1951. In June, 1952, the aneurysm was noted. Dr. McGuinness said that the case was interesting, since in spite of penicillin therapy there was objective evidence of continuation of the disease process. Admittedly the earlier courses of penicillin therapy had been of seven to nine days' duration. Throughout the serological findings had not changed. In view of the opinion that when penicillin was used in the treatment of neurosyphilis a period of fifteen to twenty-one days was advisable, it was suggested that such courses might have prevented the occurrence of the aneurysm.

Hæmochromatosis.

Dr. McGuinness then showed three patients suffering from hæmochromatosis. All had skin pigmentation, in two cases brown and in the other a slatey grey. In one case the classical triad was presented—pigmentation, *diabetes mellitus* and an enlarged liver. The other two patients had no glycosuria, and the results of glucose tolerance tests were normal. In all cases the serum iron content was elevated and the protein was saturated with iron. One of the patients was a female, who had presented with pain in the right hypochondrium, a symptom noted by Sheldon in his monograph as occurring in 6% of cases. In the French literature that symptom was noted as occurring in 34% in Boulin's series. Various suggestions had been made to explain the pain; it had been thought to be due to pancreatitis, to vasospasm due to iron deposition in smooth muscle, in cells of arteries and in the alimentary tract, and to adrenal involvement as in the premonitory phase of a crisis in Addison's disease. In the third case a diagnosis of refractory anaemia of macrocytic type had been made in 1943, and since that time the patient had received 56 blood transfusions, latterly transfusions of packed red cells only. His liver was grossly enlarged, reaching to the iliac crest, and the pigmentation was a deep slatey grey. Examination of the sternal marrow and a skin biopsy revealed iron deposition in both. In 1946 the diagnosis of hæmochromatosis had been made and confirmed by the finding of an abnormally high serum iron content and saturation of the protein with iron in 1952. The gross hepatomegaly (diffuse hepatic fibrosis) was probably due to the associated chronic anaemia, as well as to iron deposition in the liver. Dr. McGuinness said that it was probable that the development of transfusion hæmochromatosis in that case was linked with an inherent storage defect, as occurred in idiopathic hæmochromatosis. The excellent condition of the patient excluded the possibility of such factors as Gillman's malnutrition group. Treatment of the patient was designed to maintain a level of haemoglobin conformable with subjective comfort by transfusion of red cells only. The case would be reported fully later.

Portal Hypertension.

The next patient shown by Dr. McGuinness was a male, aged seventy-eight years, who had been admitted to the hospital after treatment for haematemesis. The spleen was firm and enlarged to four fingers' breadth below the costal margin and oesophageal varices were shown on radiographic examination. The liver was shrunken, but there was no objective evidence of liver diseases such as the presence of naevi, liver palms *et cetera*. The thymol turbidity was eight units, and other tests gave results within normal limits. A

previous haematemesis had occurred in 1948. An X-ray and follow-through examination with a barium meal revealed no abnormality of the gastric or duodenal mucous membrane. Blood counts revealed persistent leucopenia (2000 to 3000 leucocytes per cubic millimetre) with thrombocytopenia. The diagnosis of portal hypertension was suggested by the finding of hypersplenism and oesophageal varices. For the diagnosis of hypersplenism examination of the marrow had to reveal a normal maturation process of all series. Dr. McGuinness said that the explanation of the relatively normal results of liver function tests in the presence of portal hypertension was that the pressure on the venous radicle in such cases was probably due to regenerating liver cells, rather than to "fibrosis". The case under discussion demonstrated the need for rapid transfusion in severe haematemesis in patients in that age group, and the problems of treatment of portal hypertension. In view of the age of the patient, despite the diagnosis, the only simple surgical procedure was hepatic artery ligation, anastomotic procedures being considered too "major".

Lipoatrophy.

Dr. McGuinness finally showed a male patient, aged fifty-seven years, who had been treated for diabetes with protamine zinc insulin since 1950. About eight months earlier, atrophy of the subcutaneous tissues had been noted at the site of injection of insulin in the abdominal walls. Another brand of insulin was then used, and injections were given into the lateral aspects of the thigh as well as into the areas of lipoatrophy in the abdominal wall. However, there had been a gradual extension of the lipoatrophy to the thighs and buttocks and to the legs—in other words, to areas not the site of insulin injections. At the time of the meeting the subcutaneous tissues of the iliac fossæ, thighs and legs presented an almost symmetrical lipoatrophy. Dr. McGuinness said that the condition anatomically was the reverse of the idiopathic condition, progressive idiopathic lipodystrophy. There was as yet no definite evidence that subcutaneous tissue was increasing in the facies and chest. Suggested aetiological factors in insulin lipoatrophy were cresols, alcohol, lipolytic ferments present in insulin, and possibly nervous injury. The case under discussion was notable for the fact that injection into areas of lipoatrophy had not brought about an improvement, as was currently reported, and again for the progressive change, anatomically unrelated to the site of injection of insulin, that was occurring in the subcutaneous tissues.

Thyrotoxicosis Treated with Drugs of the Thiouracil Group.

DR. E. H. STOKES first showed three patients who had been treated for thyrotoxicosis with drugs of the thiouracil group. These patients had been shown at a meeting of the New South Wales Branch of the British Medical Association held at Sydney Hospital in 1949, and Dr. Stokes thought that it would be of interest to the members to see these patients again.

The first patient was a woman, aged twenty-one years, who had suffered from palpitation, breathlessness on slight exertion, excessive sweating and loss of weight during the previous six months. The thyroid gland was diffusely enlarged. The pulse rate was 150 per minute and the blood pressure readings were 190 millimetres of mercury, systolic, and 100 millimetres, diastolic. The eyes were prominent, but there was no exophthalmos. Fine tremor of the hands was present. The basal metabolic rate was +56%, and the serum cholesterol content was 85 milligrammes per 100 millilitres. Methyl thiouracil was given and the dosage was gradually increased until 600 milligrammes per day were being taken. The patient's condition improved, and the dosage was decreased to 300 milligrammes per day. After three months' treatment she was discharged from hospital. The highest serum cholesterol content was 281 milligrammes per 100 millilitres two months after her admission to hospital. Early in 1950 she married. She had a normal labour in 1951. During the first five months of pregnancy the administration of methyl thiouracil was continued. At the time of the meeting her general condition was excellent, and although the thyroid gland was slightly enlarged there was no clinical evidence of thyrotoxicosis.

The second patient had also been treated with methyl thiouracil. She was a woman, aged thirty-two years. The clinical features of her condition were irritability of two and a half years' duration, excessive sweating, tremor of the hands, exophthalmos and diffuse enlargement of the thyroid gland. It was of interest to note that the swelling of the gland had been present for three months, but the

exophthalmos had been observed by her relatives for six months. The pulse rate was rapid—120 per minute—and glycosuria was present. The basal metabolic rate was +44%, and the serum cholesterol content was 110 milligrammes per 100 millilitres. Methyl thiouracil in doses of up to 400 milligrammes per day was administered. The basal metabolic rate fell to +6% and the serum cholesterol content rose to 304 milligrammes per 100 millilitres. At the time of the meeting there was ~~no evidence~~ thyrotoxicosis.

The third patient was a ~~woman~~ twenty-one years, who had been suffering from ~~functional~~ instability, palpitation, excessive sweating and ~~an~~ insatiable appetite. A swelling had been present in the neck for two years. The eyes had been prominent for a similar period. There had been no loss of weight. A bruit was audible over a bilateral diffuse enlargement of the thyroid gland. A fine tremor of the hands was present, and tachycardia was noted. The basal metabolic rate was +40%, and the serum cholesterol content was 64 milligrammes per 100 millilitres. Treatment consisted of the administration of propyl thiouracil in doses of up to 200 milligrammes per day. After leaving hospital the patient married and became pregnant. During the first seven months of the pregnancy the administration of propyl thiouracil was continued. At the time of the meeting there was slight enlargement of the thyroid gland, but no clinical evidence of thyrotoxicosis.

Dr. Stokes remarked that in these three cases a remission of thyroid toxicity had occurred and it was hoped that it would be permanent.

Clinical Photographs.

Dr. Stokes then demonstrated a series of clinical photographs. The following were shown: photographs of patients showing post-operative myxedema, *leontiasis ossea*, clubbing of toes in congenital heart disease, deformity of one ear and hemiatrophy of the face, the eyes in Gaucher's disease and thyrotoxicosis (two cases); X-ray films showing evagination of the diaphragm, thoracic stomach, pleural effusion (two cases) and hydatid disease of the lung; electrocardiograms showing coupled beats resulting from the administration of digitalis, trigeminal rhythm caused by supraventricular extrasystoles, parasystole, nodal rhythm and abnormal left axis deviation; and a phonocardiogram showing an aortic "to-and-fro" murmur. Dr. Stokes said that some of the photographs had been taken by the late Mr. L. W. Appleby, photographer to the Sydney Hospital, and others by his successor, Mr. R. Money.

Recordings of Cardiac Sounds.

Dr. Stokes finally showed gramophone recordings of various heart sounds of interest. These included the sounds heard in aortic regurgitation, the *bruit de tabourka*, the machinery murmur heard after the Blalock-Taussig operation and the coupled rhythm of digitalis intoxication.

Jaundice due to Gall-Stones.

DR. J. M. YEATES first showed a man, aged sixty-one years, who had complained for three months of nagging pain in the epigastrum. At times the pain was sharp in character, but there was no suggestion of true colic. The pain was not related to food. The patient had a great desire for fatty food. He had no indigestion and no flatulence. At times nausea and vomiting accompanied the pain. The patient said that he had lost four stone in weight in the last six years. One month prior to the meeting he had noticed that his motions were pale in colour and the urine dark. For two weeks he had had itching of the skin.

On examination of the patient, it was obvious that he was jaundiced, although he himself scarcely seemed aware of the fact. There were numerous haemorrhagic spots on the skin of the abdomen. His liver was so enlarged that the edge was near the umbilicus. The gall-bladder was not palpable, and there was no significant tenderness. The urine was found to contain bile. One week later, the clinical picture was the same but the jaundice was more pronounced.

A diagnosis of obstructive jaundice probably due to malignant disease was made, and the patient was referred for operation without delay. Pre-operative treatment included the administration of 10 milligrammes of "Synkavite" per day, "Multivite" tablets, "Anahæmin" (two millilitres every second day), penicillin and blood transfusion just prior to operation. During this period certain pathological tests were performed. The Van den Bergh test gave an immediate direct reaction. The serum bilirubin content was 8.7 milligrammes per centum, the serum alkaline phosphatase content was 24.6 units, and the thymol turbidity was 12 units.

The total protein content of the serum was 6.3 grammes. The blood urea nitrogen content was 18 milligrammes *per centum*, and the total blood cholesterol content was 286 milligrammes *per centum*.

Operation was performed on June 23, 1952. The liver was found to be large and congested. The gall-bladder was enlarged, firm and white. The pancreas was firm but not hard. A large stone was found in the lower end of the common bile duct, which was slightly dilated. The duct was opened and the stone removed without difficulty from the ampulla. Probes now passed with ease into the duodenum. When the proximal part of the common duct was explored, two more stones were found and removed. The duct system was then irrigated with saline, the catheter being left *in situ* for drainage. The gall-bladder was then removed, and the abdomen closed. For some unknown reason no bile drained down the catheter until the third day, when a trickle appeared. The flow then increased daily up to about 12 ounces on the seventh day. On the eleventh day, the bile was a clear golden colour and the catheter was removed. The patient's convalescence was particularly smooth. He was discharged from hospital on the sixteenth day, when his jaundice had almost disappeared. At this stage his serum bilirubin content was 2.3 milligrammes *per centum*. Dr. Yeates said that during the three months since operation the patient had gained in weight and was now better than he had been for many years. The case showed once again the inestimable value of early operation on patients presenting with obstructive jaundice. An interesting feature was the very large liver, despite a fairly short history.

Eosinophile Granuloma of the Anus Causing Intestinal Obstruction.

Dr. Yeates then showed a boy, aged five years, who had been admitted to Sydney Hospital on June 10, 1952, complaining of a "swollen stomach" present for five days. His mother said that for one year previously he had suffered from a persistent skin lesion in the anal region. During that period his bowels had been reluctant to move, and he often went for three days without a motion even though he was in the habit of taking paraffin three times a day. He had complained of lower abdominal pain particularly at night.

Examination showed that the child was pale and obviously ill. His tongue was coated, his lips were ulcerated and his breath was foul. His abdomen was greatly distended, and large coils of bowel were visible. A plain X-ray picture of his abdomen was taken. The report stated that "there is gross distension of large bowel. The appearance is consistent with Hirschsprung's disease". Examination of the anal region revealed that the perianal skin was covered all round for three centimetres with a polypoid lesion which was bleeding slightly. When digital examination was attempted, no sooner had the sphincter been passed than a large quantity of fluid faeces was violently ejected. The child's condition improved almost at once, and the abdominal distension was much reduced. An enema given later in the evening produced more faeces. During the next few days, it was apparent that the abdomen was again becoming distended. Enemas were of little help, and the child was becoming distressed.

On June 23 a proctoscopic examination was performed under general anaesthesia. It was seen that the lesion ended quite suddenly at the mucocutaneous junction, the anal mucosa being normal. A biopsy was performed, and a number of tests were carried out. The Wassermann, Kahn and Frei tests all produced negative results. Stool examination failed to reveal parasites, cysts or ova. Examination of a direct smear revealed a few pus cells, and a culture yielded only *Staphylococcus albus* and diphtheroids. The blood count was normal. Dr. L. D. Finlay-Jones's report on the biopsy specimen was as follows: "The dermis is infiltrated with large collections of closely packed histiocytes with intermingled eosinophils. The presence of numerous mitotic figures suggests active proliferation of the histiocytes. There are lymphocytes and plasma cells at the edges of the lesion. The changes correspond with those described in eosinophilic granuloma of the skin."

On July 3 Dr. Sylvia Bray examined the patient in consultation, and reported that such lesions were usually radiosensitive. She suggested a moderate dose of X-ray therapy. That treatment was commenced on July 7, a dose of 150r being given. It was repeated on July 9, and again on July 11. The next day the child developed chickenpox and was transferred to Prince Henry Hospital. When he was examined again about one month later, the lesion had entirely disappeared. Two more doses of X-ray therapy were given on August 27 and 29.

Dr. Yeates said that at the time of the meeting, except for faint pigmentation, the skin appeared sound. No further difficulty had been experienced with bowel actions.

Gastric Ulcer Treated by Gastrectomy.

Dr. Yeates then showed a woman, aged thirty-six years, who had complained of epigastric pain and vomiting for over a year. The pain bore no relation to food, but often woke her at night. She had been admitted to a medical ward in Sydney Hospital on April 15, 1951, because of severe anaemia following persistent vomiting of black material like liquorice. This vomiting had commenced about three weeks prior to her admission to hospital. She admitted to being a heavy drinker, and said that sometimes she would drink one bottle of rum, or four bottles of wine, or ten pints of beer in one day. She smoked thirty cigarettes and drank eight cups of tea daily.

She was treated by repeated blood transfusions. A radiograph of the stomach taken after a barium meal on April 24 revealed a large ulcer crater with surrounding induration on the distal third of the lesser curve of the stomach. Medical treatment was apparently so effective that a similar examination on May 17 showed no evidence of the ulcer.

On March 15, 1952, she was readmitted to hospital because of severe weakness and persistent vomiting. Her pulse rate was 108 per minute. She looked thin, pale and worried. Her haemoglobin value was 11.4 grammes *per centum*. An X-ray film taken at the out-patient department on February 28 revealed a dilated stomach, due to pyloric stenosis from an old ulcer. After one week's treatment with a liquid diet of high protein content her condition improved, but she gained only one pound in weight. On March 25 she complained of burning pain not relieved by milk or alkalis. Daily gastric lavage was then commenced, with great symptomatic relief.

Gastrectomy was performed on April 7, when it was judged that her condition was as good as possible. The ulcer was found to be large and adherent to the liver in front and to the pancreas behind. The pathological report read as follows: "The specimen consisted of portion of the stomach 27 centimetres along the great curve and 8 centimetres along the scarred lesser curve, to which were attached numerous tags and a little tissue resembling pancreas. A chronic ulcer, 2.2 centimetres in diameter and about 0.7 centimetre deep, was situated on the lesser curve and posterior wall 2.5 centimetres from the upper edge of the specimen." Microscopic examination revealed no evidence of carcinoma. Pancreatic tissue was attached to the scar tissue on the deep surface. The patient made a good recovery from the operation and was discharged from hospital on the fourteenth day after operation.

Pyloric Stenosis Treated by Gastrectomy.

Dr. Yeates's next patient was a man, aged sixty-three years, who had suffered from pain and vomiting since 1917, soon after his discharge from the British Army. The pain was nagging in character, and was situated just below the umbilicus. It appeared about two and a half hours after food and was relieved by food and alkalis. In 1944 he had vomited some blood. This happened again in 1948, when he collapsed in the street from loss of blood. Recently his pain had been more severe and he had felt extremely weak. On April 14, 1952, he had a third hematemesis, and prior to his admission to hospital had been vomiting every day; very often there was blood in the vomitus. On examination in June, 1952, he was seen to be thin and gaunt. His abdomen was scaphoid and there was deep tenderness in the epigastrium. The report on a radiograph of his stomach after a barium meal read as follows: "There is a marked degree of pyloric stenosis, with half the meal retained at 5 hours. The nature of the obstructing lesion could not be demonstrated, but chronic ulcer is suspected."

The patient was admitted to a surgical ward on July 15. Gastric aspiration yielded a large quantity of sour-smelling, brown fluid. Gastric lavage was performed daily, and in a few days the return fluid was clear. The patient was given a high-protein, high-vitamin diet and blood transfusions.

Gastrectomy was performed on July 21, the aim being to remove the ulcer but not very much stomach. The pathological report was as follows: "The greater part of the stomach measuring 4 centimetres along the lesser and 13 centimetres along the greater curve. 1.5 centimetres from the pyloric end in what appeared to be the pylorus, there was a peptic ulcer 1 centimetre in width and 0.5 centimetre deep. The surrounding mucosa was thickened and congested. Fibrosis extended to the serous surface beneath the ulcer." Microscopic examination confirmed the presence

of a chronic ulcer of the pylorus. The base of the ulcer extended deeply into the muscle coats and was lined with granulation tissue. Many of the arteries were affected by endarteritis. There was no sign of malignant disease.

The patient developed a persistent hiccup on the third post-operative day. This failed to respond to every known cure and proved most fatiguing for several days. For a few nights he also regurgitated about two ounces of bile, usually about midnight. By the seventeenth day he was taking his food with enjoyment and was free from all symptoms. He was then discharged from hospital. At the follow-up clinic on August 20 he looked well and had gained four pounds in weight. A radiograph showed that his stomach was functioning well. He had recently walked from Central Railway Station to Sydney Hospital.

Dr. Yeates said that in the treatment of an elderly patient suffering from pyloric stenosis, gastro-jejunostomy was usually a sound procedure. In the case under discussion haematemesis was also a very important factor, and the only certain method of curing that symptom was removal of the ulcer. It was stressed that the longer and more assiduous the pre-operative treatment, the more easily and safely could such ulcers be resected. Dr. Yeates added that in the last year he had followed the technique of W. E. Tanner—the performance of gastrectomy with closure of about half the cut end and anastomosis of the other half to a loop of jejunum 15 inches from the flexure laid in front of the colon, with the afferent limb adjacent to the lesser curve ("iso-peristaltic").

Carcinoma of the Colon.

Dr. Yeates then showed a woman, aged sixty-six years, who had been born in Poland and was unable to give a very clear history. The main fact was that two weeks prior to her visit to the out-patient department she had passed blood per rectum. The motions had also been frequent and loose and accompanied by some pain in the left lower quadrant of the abdomen. Two years previously she had had a similar attack.

Examination revealed the patient to be a very obese woman, with no abnormal findings in the abdomen. No hemorrhoids were seen on proctoscopic examination. A sigmoidoscopic examination was performed the next day. The instrument passed easily to 20 centimetres, at which level resistance was felt and the mucosa appeared reddened. No definite carcinoma could be seen. A radiograph taken after a barium enema the next day was reported on as follows: "There was no obstruction to the inflow of the enema—but repeat advised because the bowel contained faeces." The examination was repeated a few days later, but failed to reveal any lesion. In view of the history and sigmoidoscopic findings (both vague but suspicious), the patient was prepared for operation by irrigation of the colon and administration of "Thalazole" for five days.

Operation was performed on March 24, when a typical ring carcinoma was found in the lower pelvic part of the colon. There were no evident metastases in the liver or elsewhere. The segment containing the carcinoma was resected and an end-to-end anastomosis was performed. Proximal colostomy was not added. The patient's bowels worked on the fifth day, and she was discharged from hospital on the twenty-second day. The pathological report on the specimen was as follows: "The specimen consisted of a segment of colon 15 centimetres long. Situated 3 centimetres from one cut end there was a carcinomatous ulcer which encircled the bowel and measured 3 centimetres in the long axis. Microscopy: The growth is an adeno-carcinoma which has extended through the muscle layers with surrounding fibrosis and chronic inflammation."

Dr. Yeates said that the clinical history served as a warning to all those who tended in the appraisal of such cases to be lulled by negative radiographic findings. Sigmoidoscopic examination of the lower eight or ten inches of the bowel was usually infallible and was always worth attempting even without preparation. If one was still in doubt, laparotomy was strongly advised.

Jaundice following Drainage of Empyema of Gall-Bladder.

The next patient shown by Dr. Yeates was a woman, aged sixty-five years, who had presented on December 4, 1951, with pain in the right upper part of the abdomen of three weeks' duration. Vomiting and diarrhea were also present. She recalled having had similar attacks twice in the preceding five years. During that period she had not complained of indigestion, but disliked fatty foods.

Examination of the patient revealed a rounded, tender mass under the right costal margin. Her temperature was 99° F. and her pulse rate 94 per minute. The leucocytes numbered only 7500 per cubic millimetre. She was diagnosed as suffering from acute cholecystitis, and was treated with penicillin and "Chloromycetin". Her temperature rose to 101° F. on December 6, and then subsided to normal. Her symptoms and signs had similarly abated.

Operation was performed on December 10, in the hope that the gall-bladder might safely be removed, so that another admission to hospital at a later date might be avoided. The gall-bladder was found to be large and tense and exuded pus when an attempt was made to handle it. Some eight ounces of pus were aspirated, and also many grey-coloured stones about 0.5 centimetre in diameter. Cholecystectomy was attempted, but abandoned because of the difficulty in defining the anatomy of the ducts. A large tube was sutured into the gall-bladder. This was removed on December 22, and the wound was healed on December 29. Culture from the pus produced a growth of *Alkaligenes faecalis*, insensitive to both streptomycin and "Chloromycetin".

The patient was readmitted to hospital on May 23, 1952, for routine cholecystectomy. She said that about two weeks after her discharge from hospital she had suffered from an attack of pain and vomiting and that jaundice had gradually appeared. This subsided under treatment by her local doctor. Operation was performed on May 26. The common bile duct appeared normal, but in view of the history of jaundice it was opened and thoroughly explored. No stones or obstruction were found. The gall-bladder was removed without difficulty. The common duct was drained for ten days. The patient was discharged from hospital, well, on June 16.

Dr. Yeates remarked that in the management of acute cholecystitis, primary cholecystectomy was possible only in the first few days before the pathological changes were gross. The case under discussion showed that even when all the symptoms had subsided, removal of the offending viscus at an intermediate stage was fraught with danger. At least three months' delay seemed advisable.

Paget's Disease of the Vulva.

Dr. A. A. Moon showed a married woman, aged seventy-one years, who had had six children. The menopause had occurred at the age of fifty-three years. The patient had had vulval irritation and swelling without discharge for five years. The irritation had increased despite extensive investigation and treatment at the skin out-patient clinic (Dr. G. Finley) for nearly three years. Treatment at the clinic had included local applications, skin X-ray therapy, the use of antihistamines, the oral administration of stilboestrol, intramuscular injections of testosterone propionate, and the oral administration of vitamin E and dilute hydrochloric acid.

On examination, the patient was seen to be in satisfactory general condition. The urine was clear. The blood pressure was 180 millimetres of mercury, systolic, and 120 millimetres, diastolic. The vulval skin was red and thickened in some areas and thin and white in other areas. The affected area extended from above the clitoris to the perianal region, and was more pronounced on the right side than on the left. The diagnosis of intractable *leucoplakia vulvae* and/or *lichen sclerosus et atrophicans* was made, and simple vulvectomy was considered to be indicated.

On March 18, 1952, simple vulvectomy with wide removal of the diseased skin was performed. Convalescence was straightforward, and the patient was discharged from hospital on April 9. She had remained free of vulval symptoms. On July 23 she reported that she was well after the operation and had had no ill effects.

The pathologist's report on a biopsy of the vulva was as follows: "Sections show hyperkeratosis, parakeratosis and irregular thickening of the epidermis. In the epidermis there are large cells with irregular nuclei and pale vacuolated cytoplasm; these cells are mainly in groups near the basal layer. Mitoses are fairly plentiful. The appearances indicate intradermal carcinoma and are more suggestive of Paget's disease of the vulva than Bowen's disease." Dr. Moon said that extramammary Paget's disease was a rare condition, and the case under discussion seemed to be the only definite case of Paget's disease of the vulva in the Sydney Hospital records. The condition first described in 1874 was still the subject of controversy. The axilla and ano-genital regions were the usual sites of extramammary Paget's disease. One theory suggested that Paget's disease in those areas was the intraepidermal metastasis from an

underlying carcinoma of the apocrine sweat glands. Clinically the vulval lesions were described as red discolouration of the skin of the labia spreading out to the groins and down to the anal region. The affected skin was usually thickened and edematous, had a definite border and was not hard.

Carcinoma of the Vagina and Associated Lung Metastases.

Dr. Moon's second patient was an unmarried woman, aged seventy years, who had been first admitted to the hospital on November 5, 1949, with the diagnosis of probable carcinoma of the vagina. She had had vaginal bleeding for six weeks. She had undergone an operation which was thought to be myomectomy fifteen years earlier, and subtotal hysterectomy three years earlier. Details of the operations were not known and sections were not examined; but the patient thought that the operations were performed for uterine fibroid tumours.

On examination of the patient, three small friable plaques of tissue were present on the lateral vaginal walls about one and a half inches from the introitus. The residual cervix was healthy and the pelvis felt normal. Examination of a biopsy specimen from the vaginal lesion revealed active chronic inflammation; there was an area suggestive of squamous carcinoma, but the findings were not conclusive. It was considered that the vaginal lesions, if carcinomatous, were probably secondary to carcinoma elsewhere. Investigations directed towards finding a primary growth were carried out, with negative results. X-ray examination of the chest revealed several small areas which appeared to be metastatic growth, but old tuberculous lesions could not be excluded. X-ray examination after a barium meal and a barium enema and an excretion pyelogram revealed no abnormalities. The patient was allowed home under observation.

She was readmitted to hospital on February 9, 1952 (nearly three years later), with a history of vaginal bleeding of three months' duration, incontinence of urine, and a cough for one year. There was little alteration in her general condition of health, which was relatively good. Examination and vaginal biopsy on August 13 showed that the vaginal wall was almost covered by friable and bleeding neoplasm. This extended from just inside the introitus to the vault, but did not involve the *cervix uteri*. The pathological report on the sections of tissue was as follows: "Poorly differentiated carcinoma with many regions of necrosis. In one situation the growth tends to have a glandular arrangement and other parts are suggestive of squamous carcinoma. The pattern is not distinctive enough to provide evidence of the site of origin of the growth." At the time of the meeting X-ray films of the chest revealed many shadows throughout the lung fields suggesting numerous metastases. Cystoscopic examination and excretion pyelography revealed no abnormalities.

Dr. Moon said that primary carcinoma of the vagina was a rare neoplasm, and was usually a squamous-cell carcinoma. Secondary carcinoma of the vagina was found with primary disease in organs such as the body of the uterus, the ovary, the kidneys and the breasts. The anterior vaginal wall at an area one centimetre from the urethral meatus was a recognized site for such metastases. No primary lesion had been found in the case under discussion. The histological picture of the vaginal neoplasm was atypical and did not suggest the site of the primary growth. Despite a history of growth involving the vagina and the chest for over three years, the patient's general condition had remained much the same. Chest symptoms and signs were few despite the gross lung metastases shown radiologically.

Giant Intracanalicular Fibroadenoma.

DR. T. E. WILSON showed a married female patient, aged fifty-two years, who had complained of the presence of a lump in the left breast for twenty-two years; it had been increasing in size for twelve months, but she had no other symptoms. On examination of the patient, a nodular mass measuring about six by four by four inches was found in the upper, inner quadrant of the left breast; it was not adherent to the skin or to the deeper structures.

On August 2, 1952, left simple mastectomy was performed. The pathologist reported as follows on the specimen:

A cylindrical segment of breast 9.0 cm. long and 9.0 cm. in diameter was received. Most of the specimen was occupied by a lobulated circumscribed lesion measuring 9.0 cm. x 8.5 cm. x 6.0 cm. The cut surface showed pink slightly translucent tissue with tiny cysts.

Microscopic examination: The growth has the structure of a giant intracanalicular fibroadenoma. Hyaline and myxomatous change are present in the connective tissue stroma. Some regions are fairly cellular, but mitoses are few and no convincing evidence of malignancy has been found.

Multiple Injuries.

Dr. Wilson's next patient was a man, aged twenty-two years, who on May 17, 1952, had been hit in the left loin by an elbow while he was playing football. He stopped playing for a few minutes, but resumed the game. He had mild pain for the next six hours, then more severe pain. On examination of the patient, considerable tenderness was present in the left loin and beneath the left costal margin. His pulse rate was 88 per minute and he was very pale. His blood pressure was 130 millimetres of mercury, systolic, and 90 millimetres, diastolic. His urine was not blood stained. The haemoglobin value was 8.6 grammes per centum.

At operation, nine hours after the injury, a left upper abdominal oblique incision was made and the ruptured left kidney and spleen were removed. Left hemicolectomy was also performed because of extensive bruising of the descending colon. A large retroperitoneal haematoma was present. The bowel ends were brought out as a spur colostomy, and a transfusion of two litres of blood was given. The post-operative course was uneventful. The spur was crushed and the colostomy closed on July 16.

Imperforate Anus.

Dr. Wilson's third patient was an infant, who had been born on November 4, 1951, at full term after a normal pregnancy. The external opening of a recto-perineal fistula was found at the junction of the scrotum and perineum, and there was a slight dimple at the normal site of the anus. Some contraction of the underlying external sphincter muscle occurred on stimulation of the perineal skin. Meconium and then faeces were passed through the fistula.

At operation on November 14 a sagittal incision was made in the perineum. A fistulous track (about one and a half inches long) was dissected out, the lower end of the rectal stump was found and mobilized (Ladd and Gross type III deformity), and the rectal mucosa was sutured to the perineal skin with catgut. The wound was dressed with "Vaseline" gauze. Post-operative dilatation of the "anus" was performed weekly for two months, and then at increasing intervals. At the time of the meeting the anus gaped on traction with the finger, although there was fairly good tone in the external sphincter.

Endometriosis of the Rectum.

Dr. Wilson's next patient was a woman, aged fifty-nine years, who had been admitted to Sydney Hospital on May 5, 1952, and discharged on August 9. She had suffered from pain and swelling in both legs for two years, more severe for twelve months. She had had severe pain in the back for twelve months, coming on at night and lasting for a few days, and had been weak and tired for six months. Her bowels were open regularly. Rectal bleeding had occurred once three months before her admission to hospital.

On examination of the patient, both her legs were hot and sweating and the right ankle and leg were swollen. The arterial pulses were palpable at the ankles. Homan's sign was absent. Occasional extrasystoles occurred. An electrocardiogram revealed a myocardial defect. Vaginal and rectal examination revealed a hard mass in the posterior fornix, separate from the uterus. On sigmoidoscopic examination a protruding mass was seen at 15 centimetres; the overlying mucosa was intact.

Before her admission to hospital, the patient was treated by rest, a course of heparin and mersalyl injections. Before operation, phthalylsulphathiazole (12 grammes daily) was given for four days. Streptomycin was given by mouth (one gramme daily for two days), and a daily enema was given for three days.

At operation on May 20 a hard mass was felt in the recto-vaginal septum resembling carcinoma of the middle third of the rectum infiltrating the cervix. Total hysterectomy and resection of the sigmoid colon and the upper part of the rectum were carried out.

The pathologist reported that the specimen consisted of the uterus, including the cervix, together with part of the rectum and sigmoid colon measuring 23.0 centimetres in length. The bowel was joined to the posterior surface of

the uterus opposite the endocervical canal by a nodule of leathery fibrous tissue measuring approximately 3·0 by 2·0 by 2·0 centimetres. In the cut surface there were some small cysts measuring up to 0·3 centimetre in diameter, some of them containing brownish fluid. There was no evidence of ulceration in the mucosa of the bowel, and the wall was not thickened. The uterus measured 7·0 by 4·0 by 2·5 centimetres, and a small polypus 1·5 centimetres long projected into the uterine cavity. Microscopic examination of the sections revealed endometriosis of the wall of the rectum and cervix, and there were endometrial islets in the intervening fibrous connective tissue. In some of the endocervical glands there were small regions of squamous metaplasia. An unusual gland with vascular and cellular surrounding connective tissue somewhat resembling a *theca folliculi* was present in the endocervix. There was recent haemorrhage in the stroma of the endometrial polypus.

Pulmonary embolism occurred on the sixteenth day after operation, and was followed the next day by the signs of deep venous thrombosis in the right leg; 140,000 units of heparin were given intravenously over the next six days; then the administration was discontinued. A second right venous thrombosis occurred three days later, and heparin therapy was recommended; despite the treatment a pulmonary embolism occurred six days later. Heparin to a total dose of 1,060,000 units was given over the next twenty-eight days until the patient was ambulant and the colostomy spur had been crushed. The colostomy was closed on July 29. The patient was discharged to a convalescent home two weeks after closure of the colostomy, at which time the wound was healed and the bowels were functioning normally.

Ano-Rectal Fistula.

The next patient shown by Dr. Wilson was a man, aged forty-five years, who in 1947 had had haemorrhoids injected. In September, 1949, drainage of an ischio-rectal abscess had been carried out. The discharge ceased three weeks later, but recurred after another month and had persisted since then. In March and May, 1950, operations for anal fistula were performed, but without effect on the discharge.

On May 31, 1952, the patient was admitted to Sydney Hospital. There was an external opening about one and a half inches to the right of the anus posteriorly. The fistulous track was not palpable through the skin. There was an area of induration in the region of the ano-rectal ring in the mid-line posteriorly, but the internal orifice of the fistula was not palpable.

On June 3 the bilateral fistulous tracks on the under surface of the pubo-rectalis muscle were laid open and the anal canal was divided down to the internal opening, which was situated between the deep part of the external sphincter and the pubo-rectalis. The resulting wound was about five inches in diameter, and its walls were flat and shelving. On July 25 the patient was discharged home; at that stage the wound measured about one inch by one-quarter of an inch. Dr. Wilson said that the resulting scar was about two inches long on each side of the anus and about an eighth of an inch wide; but it was still unstable and apt to crack on exercise. It should soon become more resistant and would remain healed. It was considered that no further recurrence of the fistula was possible.

Idiopathic Rectal Stricture.

Dr. Wilson then showed a female patient, aged sixty-two years, married, and the mother of two children, aged forty-seven and forty-five years respectively. She had been well till 1945, when she first complained of precipitancy of defaecation with passage of blood *per rectum* and colicky lower abdominal pain. She had not lost weight. In 1947 she had undergone radical mastectomy for carcinoma of the right breast. On examination of the patient in 1947, the anus was in spasm. There was a tubular stricture two inches from the anal margin. The patient had a very large non-toxic adenomatous thyroid gland. On January 13, 1948, an X-ray examination of the chest and radiological examination with a barium enema revealed no abnormality. On January 15 no cysts or ova were seen in faeces, and there was no eosinophilia. The rectum was dilated digitally in January, 1948, with relief.

On February 24, 1949, the patient was admitted to hospital because of increased lower abdominal pain and bleeding *per rectum* for three weeks. Under "Pentothal" anaesthesia one ounce of pus was expressed from the anus, and the stricture was dilated. The lumen of the stricture was ulcerated; no amoebae or cysts were found in a scraping from

the surface of the ulcers, the mucosa above the stricture was pale and showed localized ulceration. Whilst in hospital the patient was given phthalylsulphathiazole (two grammes every four hours for seventeen days), "Trisulpha" (one gramme every four hours for nine days), penicillin (50,000 units every three hours for nine days), and emetine hydrochloride (one grain daily for ten days). On February 28 and March 14 examination of the faeces revealed numerous pus and epithelial cells, but no cysts or amoebae were seen. No pathogens were isolated on culture. On April 6, in a swabbing from the rectum numerous pus cells were found. There was a mixed bacterial flora. No gonococci were seen. On April 14 the Frei test produced a negative result.

On May 5, 1952, the stricture was dilated under "Pentothal" anaesthesia. On May 14 the Wassermann and Kahn tests produced negative results. On May 12 the following report was given on a biopsy of anal tissue: "Two pieces of firm tissue each approximately 0·7 centimetre in maximum extent. Microscopic examination—sections show edematous hemorrhagic vascular granulation tissue, leucocytes, and plasma cells. One section included some fibrous submucosa and a little plain muscle. The inflammatory changes have no specific histological features."

On October 24, 1950, total thyroidectomy was performed under local anaesthesia because of pressure symptoms. Dr. Wilson said that for the last three years the patient had attended the rectal clinic at Sydney Hospital every three or four weeks for dilatation of the stricture. It was now possible to pass an index finger through the stricture, which was now only about an eighth of an inch long.

Periosteal Fibrosarcoma.

DR. R. J. W. MALCOLM showed a male patient, aged thirty-six years, who had been admitted to Sydney Hospital on July 19, 1952, complaining of pain, swelling and stiffness of the left knee for six months with occasional severe pain. A biopsy specimen had been examined on June 11, and the following report given: "Microscopic sections from fatty tissue show this to be fat and synovial membrane with inflammatory cells suggesting the picture seen in rheumatoid arthritis. Sections from curettage show fragments of bone, cartilage and connective tissue densely infiltrated with inflammatory cells. No evidence of malignancy seen."

On examination of the patient on his admission to hospital, the left knee was enlarged and warm; the range of movement was 90° to 180°; there was an effusion in the joint, and slight wasting of the quadriceps. An X-ray examination showed no abnormality in the chest, and the ankle joint to be regular; there was considerable diffuse atrophy of the knee joint with periosteal new bone formation on the distal femoral shaft. Examination of a biopsy specimen from a left inguinal lymph gland (July 28) revealed moderate fibrosis, sinus catarrh, and occasional pigment-laden cells lining dilated sinuses. There was some extravasated blood in the node and outside the capsule. The vessels were congested. There was no evidence of malignancy. Aspiration of the knee joint was performed on July 28, and examination of a direct smear of the fluid revealed a moderate number of pus cells, but no organisms. Culture produced no growth of organisms. An X-ray examination on August 16 revealed appearances very suggestive of osteogenic sarcoma of the femur. Examination of a biopsy specimen from the lateral femoral condyle (September 2) revealed sarcoma, the site of origin not being determined; there was considerable infiltration with lymphocytes.

On September 7 mid-thigh amputation was performed.

Carcinoma of the Antrum of Highmore Treated by Excision of the Maxilla.

DR. FRANK ELLIS showed a female patient, aged seventy-three years, who on February 15, 1952, complained of a blood-stained nasal discharge, especially on the right side, present for a period of six months. She also complained of nasal obstruction on the right side, and of loss of the sense of smell. On examination of the patient a large, soft, necrotic mass was present completely filling the right nostril; it bled easily. A tumour could be seen in the posterior right choana. A provisional diagnosis of malignant neoplasm was made. On February 19 an X-ray examination of the sinuses revealed pansinusitis on the right side. On February 22 examination of a biopsy specimen revealed necrotic tissue only. On April 23 examination of a further biopsy specimen showed it to consist of diffuse sheets of carcinomatous cells; their histological structure was consistent with an origin from the nasal mucosa.

At operation on April 23 the right maxilla was removed. The right external carotid artery was first ligated. A lateral rhinotomy incision was made around the lateral aspect of the nose as far as the philtrum. The philtrum was split through the full thickness of the lip. The upper end of the incision was extended laterally below the right lower eyelid for half its distance. The skin and facial muscles were raised in one flap; the bone was cut through the premaxilla, through the frontal process of the maxilla, and laterally through the space between the tuberosity of the maxilla and the pterygoid process. The hard palate was then cut down the mid-line as far back as the soft palate. The soft palate was detached. The floor of the nose was sectioned close to the septum, just medial to the tumour, and the whole maxilla was rocked out. Some tumour remnants could be seen in the ethmoid region; they were removed as far as possible, the cavity was packed and the wound was closed. The patient's post-operative condition was satisfactory. Primary healing took place.

Pathological examination of the excised right maxilla on April 24 was as follows. A polypoid growth was present filling the antrum; sections were cut from one piece. Microscopic examination of the sections showed the tumour to be an epidermoid carcinoma, which appeared to arise from the antral mucosa. The structure was somewhat undifferentiated, and the findings suggested a moderate to severe grade of malignancy for tumours of that type.

The patient was discharged from hospital on May 31 with a prosthesis made at the Dental Hospital, Sydney; it occluded the opening in the palate. She was sent to the radium department at Sydney Hospital for radiation therapy. The irradiation given consisted of 10×2.4 millericuries of radon for twenty-four hours given over seven days, on a lead platform mounted on top of the prosthesis. The distance was 0.5 centimetre from the ethmoidal region.

Dr. Ellis said that the patient was able to speak and swallow normally, the wound had healed well and there was no external deformity. On July 11 some granulation tissue was noticed in the anterior wall of the cavity; it was removed and examined. The pathologist reported that the specimen consisted of three fleshy fragments; half of each was examined in sections. They consisted of granulation tissue surmounted by hyperplastic transition epithelium. Occasional epithelial glandular acini could be seen in the granulation tissue, but they appeared to be of benign structure, and no residual tumour tissue could be seen. On August 28 more granulation tissue was removed from the same place. Microscopic examination of sections showed the fragment to consist of loose connective tissue surmounted by transitional epithelium and containing scattered inflammatory cells and mucous glands. No recurrence of malignant tissue could be seen.

Dr. Ellis said that in such a case as that under discussion excision of the maxilla offered an alternative to the only other effective remedy—irradiation given either primarily or after more conservative surgery. One great advantage of the method of treatment employed was that the cavity left gave good access for inspection for any evidence of recurrence.

Adamantinoma of the Right Maxilla.

DR. V. D. BEAR showed a male patient, aged sixty-nine years, who had complained of "bleeding from a hole in the upper gum"; lately he had also had some pain in the region and swelling of the right cheek. He had apparently sustained a fracture of the right maxilla twenty years earlier with subsequent removal of his right upper canine tooth, the socket of which had never healed. He had had intermittent bleeding from the fistula and also epistaxis. There was no cervical glandular enlargement. A fistula was seen in the upper right alveolus, and in the floor of the maxillary sinus friable-looking tissue was visible, some of which was removed and sent for biopsy. The pathologist reported that the growth was composed of cords and papillae of closely packed columnar epithelium with intervening stellate reticulum suggesting that it was an adamantinoma. An X-ray examination of the sinuses suggested that there was some bone destruction in the posterior part of the right upper alveolus. The sinus films showed that that region was surrounded by a densely opaque area, which appeared to be reactive new bone.

The patient was treated with deep X rays, and then a partial right alveolectomy was performed. A dental obturator containing radon was inserted, and the patient received a tumour dose of approximately 6600r. The tissue removed at operation was reported upon as an adam-

tinoma. Since the operation and radiotherapy the patient had been well and symptom-free.

Carcinoma of the Tonsil with Metastases in the Lung.

Dr. Bear then showed a male patient, aged seventy years, who had complained of a "lump" on the left side of his neck which he had noted approximately ten to twelve months earlier, and which had become rapidly larger in the last two months. Pain was referred to the left ear. In the last two months he had been troubled with slight difficulty in swallowing, and had had some regurgitation of food and also overflow of saliva. Though his speech was somewhat slurred (possibly owing to the excessive saliva), he had had no loss of voice. He had lost approximately two stone in weight in the last twelve months.

On examination of the patient, his general condition was very fair and he was mentally alert. A hard, fixed mass was present at the angle of the left mandible, the largest gland measuring about 3.5 by 1.5 inches. A large mass with ulceration of the anterior pillar and tonsil was found on inspection. Mirror examination revealed no evidence of involvement of the hypopharynx or larynx. Examination of a biopsy specimen confirmed the presence of poorly differentiated carcinoma, which in places appeared to be of squamous epithelial origin.

The patient was treated with deep X rays, receiving a total of approximately 6600r to the left side. He experienced great relief of symptoms and also of the local lesions. He returned approximately eight months later complaining of increased difficulty with swallowing. X-ray examination by means of a barium bolus revealed no abnormality in the oesophagus, but a multitude of large metastases were seen in the lung fields. A direct endoscopic examination revealed no abnormality in the larynx or bronchial tree, but there was an obstruction approximately ten inches down the oesophagus, the appearance suggesting enlarged glands in the mediastinum. Dr. Bear said that the patient's general condition had deteriorated, as had his mental alertness. Ulceration of the left tonsil had recurred.

Lesions of the Vulva.

DR. S. D. MEARES showed a series of colour photographs illustrating various lesions of the vulva, and discussed the diagnosis and treatment. Included in the series were photographs of acute and chronic vulvitis, ulcers both single and multiple, kraurosis, leucoplakia and epithelioma. Dr. Meares said that so that diagnosis could be accurate, it was often best to take a biopsy before commencing treatment.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

AN INQUIRY FROM THE ROYAL COLLEGE OF PHYSICIANS.¹

Colonial Secretary's Office,
Sydney,
22 Dec., 1829.

James Bowman, Esq.,
Inspector of Hospitals,
Sir,

I am directed by His Excellency the Governor to refer to you the accompanying copy of a Paper transmitted with the Under Secretary of State's circular letter of the 31st May 1829 from the Royal College of Physicians containing certain questions, in order that you may reply to them as far as has fallen within your observation and the means of your Department may enable you to do.

For the Colonial Secretary,
T. C. HARINGTON.

Questions proposed by the Royal College of Physicians London (1829).

- What is the population of the Place?

¹ From the original in the Mitchell Library, Sydney.

2. What proportion do the Annual Deaths bear to the Population?
3. Are there any remarkable instances of longevity amongst the Inhabitants?
4. What are the features, complexion, colour of skin, and average Stature of the Natives?
5. What is the medium height of the Thermometer in the Summer and Winter Months?
6. From what Quarter do Winds chiefly prevail, and in what Months?
7. What is the nature of the Soil?
8. Are there any mineral Springs there? If so are they saline, chalybeate, sulphureous or of what nature?
9. What are the medical substances of the Country and how are they prepared?
10. What diseases prevail there?
11. In what seasons of the Year does Illness most prevail and what are the diseases incidental to the seasons?
12. What remedies do the natives employ in the diseases to which they are subject?
13. What is the Education of those who practise Medicine?
14. Have the Natives any writings or traditions on medical subjects?
15. What is the Diet of the Natives?
16. Do they practise vaccination? If so whence do they obtain the lymph?

Correspondence.

DOCTORS AND THE NEEDS OF THE COMMUNITY.

SIR: Owing to illness I am now only catching up with my journals of the last eight weeks, hence the delay in noticing a letter by Dr. E. S. Meyers under the above heading in the issue of December 6, 1952.

He refers to an inquiry on this subject made by the Department of Labour and Industry, to whom he supplied certain information presumably with regard to Queensland. As far as New South Wales is concerned, the first intimation that any such inquiry was being made was receipt of "A Preliminary Report on the Absorptive Capacity of the Medical Profession in N.S.W." which was dated October 8, 1948. Representations were made to the Regional Director for New South Wales of the Commonwealth Employment Service of the Department of Labour and National Service taking exception to some of the statements made in this report and drawing attention to certain anomalies and errors. Later I wrote the Special Article on "Overcrowding the Medical Profession in New South Wales" published in the journal of December 18, 1948. In 1950 a redrafted and modified "Preliminary Report" was received dated October, 1949, and early in 1951 a "Brief Review of the Absorptive Capacity of the Medical Profession in Australia" came to hand dated December, 1950. Note that it is now Australia and not merely New South Wales.

In the report of the Federal Council of the British Medical Association published in the journal of April 21, 1951, came the real explanation of these reports in a letter from the Minister for Immigration asking the Council's views on "the need for and the practicability of obtaining some greater measure of recognition of the medical qualification of foreign migrants and the manner in which such liberalization could best take place". This letter was considered at the meeting in September, 1950, and a "Migrant Doctors' Committee" was appointed to report on the matter. Dr. A. J. Collins, on behalf of this committee, made some observations and concluded by saying the problem was a large one and the committee would not be able to present a final report for some months. Dr. H. R. R. Grieve detailed the terms of reference of the committee which were rather illuminating in the breadth of their scope. Dr. T. Giblin, Dr. Angus Murray and Sir Victor Hurley also commented, and it was resolved "to report to the Minister along the lines of the information furnished by members of the committee consistent with the preliminary letter sent to the Minister by Sir Victor Hurley and that a copy of the report be sent to the Branches for their information".

As Dr. Meyers remarks, nothing has been heard of anything further being done, although one must conclude that the matter is still in the hands of the Federal Council.

As each State has its own *Medical Practitioners Act* administered under the State Minister of Health by a State Medical Board, it is not possible for Commonwealth authorities to move in the matter of facilitating registration of foreign doctors other than by requesting each State Government to alter its medical Act along parallel lines. One notices in the lay Press from time to time that various Ministers, both Federal and State, have received delegations from these foreign gentlemen and no doubt further representations will continue to be made. I was given to understand that these inquiries as to absorptive capacity were being conducted regarding all professions and trades so as to facilitate the choice of immigrants for various types of work and to aid in their assimilation into the community. These reports as to absorptive capacity of the medical profession have been based on the anticipated increase in population of 180,000 immigrants *per annum*, but as far as I can ascertain this figure has never been reached, the best year being 1950 when the net increase was 152,505 out of a total of 174,540 for the year. Since then the figures have fallen greatly.

As regards New South Wales, there is provision for foreign doctors to obtain a degree of the University of Sydney by passing an examination in the third year subjects and then proceeding through the remainder of the course, or they can qualify for practice in this State only by passing the examinations for the last three years of the medical course. The latter is the favoured choice and for some years past there has been an average of at least 16 per year entering the university, so that New South Wales is receiving the bulk of these New Australians. There is an increasing number of medical men entering Australia from Great Britain and Ireland. The numbers of students entering medicine have not fallen off as was anticipated, so taken all round our Australasian universities and British newcomers can provide more than enough doctors for the needs of our community, even allowing for the very low figure of one doctor per 800 of population. Let us hope that the Federal Council will not allow the matter to be shelved, but will bring the position very forcibly before both Commonwealth and State Governments.

Yours, etc.,
HUGH R. G. POATE.

225 Macquarie Street,
Sydney,
January 13, 1953.

A COLLEGE OF GENERAL PRACTITIONERS.

SIR: During my recent visit to London I had the pleasure of meeting Dr. John Hunt, who is the honorary secretary of the General Practice Steering Committee and an energetic worker for the formation of a College of General Practitioners, which came into being on January 1, 1953. I feel sure there is scope for such a college in Australia, and if possible a branch of the college in England.

By air mail last week I received from Dr. Hunt extracts from the *British Medical Journal* and *The Lancet* dated December 20, 1952. Leading articles in both journals support the formation of this new college, and the *British Medical Journal* prints a full report of the Steering Committee embracing the functions and criteria for membership of the college. I would urge all general practitioners to read these articles when the journals arrive in Australia and organize themselves in localities and States for the establishment of a college in Australia.

Yours, etc.,
W. A. CONOLLY.

Main Street,
Cessnock,
New South Wales.
January 7, 1953.

SECTION OF OCCUPATIONAL MEDICINE (BRITISH MEDICAL ASSOCIATION, NEW SOUTH WALES BRANCH).

SIR: The annual meeting of the above Section will be held at 8 p.m. on Monday, February 2, 1953, in the Lecture Theatre, School of Public Health and Tropical Medicine, University of Sydney. At the conclusion of the business portion of the meeting a short programme of films will be screened, and supper will be served.

During 1952 successful meetings relating to "Industrial Dermatitis" and to "Rehabilitation and Placement of the Incapacitated Worker" have been held. It is hoped that in the coming year meetings on "Medical Aspects of Workers' Compensation", "The Heart in Relation to Work" and "Radiation Hazards" will be arranged.

The committee is particularly desirous that as many general practitioners as possible should join the Section of Occupational Medicine, membership of which is open to all members of the British Medical Association.

A cordial invitation is therefore extended not only to existing members of the Section, but also to other practitioners wishing to join the Section, to be present at the annual meeting on February 2, 1953.

Yours, etc.,

GORDON C. SMITH,
Honorary Secretary.

C.O. School of Public Health and Tropical Medicine,
University of Sydney,
December 30, 1952.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

SUMMARY OF COURSES, 1953.

Courses for Higher Degrees and Diplomas.

Part I.

CLASSES in anatomy, physiology, pathology and pharmacology will be conducted on Monday and Wednesday afternoons, anatomy classes commencing on February 2 and physiology and pathology classes on March 2. Physics classes will be held on Thursday afternoons, commencing March 5. These courses will continue till August. The

fees are £31 10s. for the whole of Part I, or £15 15s. per subject.

Part II.

M.D. Part II and M.R.A.C.P.—Clinical demonstrations suitable for candidates for M.D. Part II and M.R.A.C.P. will be conducted at different hospitals on Tuesdays and Fridays as follows: haematology, February 3 to 20; neurology, March; pediatrics, March 24 to April 17; thoracic diseases, April 21 to May 8; endocrinology, May 12 to 29; cardiology, June 2 to 19; gastro-intestinal disorders, June 23 to July 7; renal disorders, July 10 to 28. The fee for each of these courses is £3 3s.

F.R.A.C.S.—A course of higher surgical instruction suitable for final F.R.A.C.S. candidates will commence on March 16 and continue till May 1. It will consist of twenty-five clinical demonstrations, on Mondays, Tuesdays, Wednesdays and Fridays, from 3 to 5 p.m., conducted at Saint Vincent's, the Alfred, the Royal Melbourne and Prince Henry's Hospitals. The fee is £21.

D.G.O. Part II.—General pathology classes for D.G.O. Part II candidates will be held on Monday and Wednesday afternoons, March to June, from March 2 at 1.45 p.m. Special pathology and bacteriology classes will be held at times to be arranged.

D.O. Part II.—Courses in ophthalmology, pathology and bacteriology for D.O. Part II candidates will be arranged when sufficient candidates present.

D.L.O. Part II.—Pathology classes for D.L.O. Part II candidates will be held on Monday and Wednesday afternoons, from March 2 till June. Bacteriology, laryngology and otology classes will be arranged when sufficient candidates present.

D.D.R. Part II.—Commencing in April, the Post-Graduate Committee, in consultation with the College of Radiologists, will conduct a course in radiodagnosis if sufficient candidates present.

D.T.R. Part II.—Pathology classes for D.T.R. Part II candidates will be held on Monday and Wednesday afternoons, from March 2 till June, at 1.45 p.m. Physics and radiotherapy classes will be held at times arranged when sufficient numbers present.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 20, 1952.¹

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism ..	1(1)	1	2
Amoebiasis	3(3)	3
Ancylostomiasis
Anthrax
Bilharziasis
Brucellosis
Cholera
Chorea (St. Vitus)
Dengue
Diarrhoea (Infantile) ..	20(18)	..	20(20)	1	..	41
Diphtheria ..	4(1)	8(6)	7(1)	1(1)	3(2)	1(1)	22
Dysentery (Bacillary)	3(2)	4(4)	9
Encephalitis
Flariasis
Homologous Serum Jaundice
Hydatid
Infective Hepatitis	8
Lead Poisoning
Leprosy
Leptospirosis	1	1
Malaria	1(1)	1
Meningococcal Infection ..	5(3)	2	..	1(1)	1(1)	3	12
Ophthalmia
Ornithosis
Paratyphoid
Plague
Pollomyelitis ..	22(8)	19(8)	4	12(7)	1(1)	11(3)	69
Puerperal Fever
Rubella	117(78)	1	118
Salmonella Infection
Scarlet Fever ..	14(9)	40(33)	6(5)	6(2)	2	68
Smallpox
Tetanus
Trachoma
Trichinosis
Tuberculosis ..	36(25)	69(52)	11(7)	11(8)	7(5)	5(3)	..	2	141
Typhoid Fever
Typhus (Flea-, Mite- and Tick-borne)
Typhus (Louse-borne)
Yellow Fever

¹ Figures in parentheses are those for the metropolitan area.

Courses for General Practitioners.

Gynaecology and Obstetrics Refresher Course.

A gynaecology and obstetrics refresher course will be conducted from August 31 to September 11. This course will be held at the Women's Hospital, Carlton, and will consist of daily ward rounds conducted in groups, at which the routine work of the hospital will be demonstrated, and of a series of lectures. Residence at the hospital during the period is advised and will be available. Fees for tuition will be £10 10s., payable to the Post-Graduate Committee, and for residence will be £6 6s. per week, payable to the hospital.

Country Courses.

Country courses will be conducted throughout the year in different centres. They will be available to all medical practitioners, and application to attend should be made to the Secretary of the appropriate British Medical Association Subdivision. Detailed programmes will be published later for each month. The centres and dates are as follows: Ballarat, February 26, evening lecture; Hamilton, March 7, evening lecture; Mooroopna, March 14-15, week-end course; Yallourn, April 18-19, week-end course; Bendigo, May 9, week-end course; Hamilton, May 23, evening lecture; Ballarat, May 28, Dr. Kate Campbell; Mooroopna, July 18-19, week-end course; Hamilton, July 25, evening lecture; Ballarat, August 27, evening lecture; Hamilton, September 5, evening lecture; Bendigo, October 10, two lectures; Horsham, October 10-11, week-end course; Hamilton, November 14-15, week-end course; Ballarat, November 26, evening lecture.

A course will be held at Flinders Naval Depot, by arrangement with the Royal Australian Navy, on the second Wednesday of February, March, April, May, June, August, September, October and December. The November demonstration will be given on November 18.

Certain overseas lecturers will visit and lecture at country centres. Details of arrangements will be published later.

Courses by Overseas Lecturers.

Dr. Macdonald Critchley, neurologist at King's College Hospital, physician at the National Hospital and Dean of the Institute of Neurology, London, will lecture in Melbourne on neurological problems from March 8 to 29.

Dr. R. D. Lawrence, physician-in-charge of the Diabetic Department, King's College Hospital, London, will lecture in Melbourne between March 21 and 28, approximately.

Dr. Douglas Guthrie, surgeon at the Edinburgh Ear and Throat Infirmary, consulting aural surgeon at the Royal Hospital for Sick Children, and lecturer in the history of medicine at the University of Edinburgh, is expected to visit Melbourne about October and give several lectures.

Sir Allen Daley, medical officer of health to the County of London, member of the Central Health Service Council and member of the British Post-Graduate Medical Federation, will arrive in Melbourne under the auspices of the Nuffield Foundation early in February. He will lecture at Warrnambool on the evening of February 14 and at Ballarat on the evening of February 17. Local arrangements are in the hands of the subdivisional secretaries.

Further Information.

Detailed monthly programmes of the committee's activities will be published in THE MEDICAL JOURNAL OF AUSTRALIA, and these will contain any arrangements made which are additional to the above. A printed syllabus of medical post-graduate facilities available in Melbourne and Victorian country centres in 1953 may be obtained on request from the committee's office at 394 Albert Street, East Melbourne.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Clinical Meeting at Balmoral Naval Hospital.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a clinical meeting will be held at the Balmoral Naval Hospital on Tuesday, February 10, 1953, at 2 p.m., when Dr. T. M. Greenaway will speak on "Some Medical Experiences Abroad". Clinical cases will be shown after the lecture. All members of the medical profession are cordially invited to attend.

Deaths.

THE following death has been announced:

OLIPHANT.—Francis Carlton Oliphant, on December 27, 1952, in England.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Clifton, Bruce Stewart, M.B., B.S., 1952 (Univ. Sydney), 4 Oaklands Avenue, Summer Hill, New South Wales.
Meredith, John Evan, M.B., B.S., 1952 (Univ. Sydney), 52 Raglan Street, Mosman, New South Wales.
Hughes, Joan Eleanor, M.B., B.S., 1952 (Univ. Sydney), 297 Edgecliff Road, Woollahra, New South Wales.
Nicholas, Judith Nella, M.B., B.S., 1952 (Univ. Sydney), 60 Kensington Road, Summer Hill, New South Wales.

Diary for the Month.

JAN. 28.—Victorian Branch, B.M.A.: Council Meeting.

JAN. 30.—Queensland Branch, B.M.A.: Council Meeting.

FEB. 3.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association; Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

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